The Journal

OF THE

AMERICAN ASSOCIATION OF NURSE ANESTHETISTS

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1. *Goodman, L., and Gilman, A.: The Pharmacological Basis of Therapeutics, New York, The Macmillan Co., 1947, p. 58.*

OPINION REVIEW

[Reader participation in this column is invited. Send your contribution to "Opinion Review," Journal A.A.N.A., 22 East Division St., Chicago 10, Illinois.]

What Price "Free" Medical Care

This comment on compulsory health insurance makes no pretense at being a learned discussion. One of the reasons for its being written is that, in the mind of almost everyone I have met, there seems to be only a vague realization that some legislation is about to be enacted by the Congress that would alter the status of the entire medical profession in its relation to the public and its health.

To those who advocate legislation of a compulsory insurance, the idea is tendered as a panacea. To those who are against it, it is being portrayed as the essence of all evil. Because of this, the general public, which includes you and me, is forced to accept or refuse the plan in its entirety. The only source of optimism is an alternative bill that either faction could accept without losing face. This bill is the Voluntary Health Insurance Bill, listed as S. 1456, which is being sponsored by Senator Lister Hill, with Senators O'Conor, Withers, Aiken, and Morse as co-sponsors. S. 1456 allows for the extension of health services within the framework of the present system.

The daily papers are filled with articles about compulsory health insurance. Lay magazines and medical journals are giving up valuable space to the subject. Radio programs give it a high public-interest rating. This would seem to indicate a very high personal interest. Yet this is not true. The average person can talk about it in only the most limited terms; the spokesman who can out-talk and out-wit the opposition will win his objective.

Despite this fact, neither side has much concrete ammunition to offer in the argument. After listening to countless radio discussions, I find that—without other sources of information—I could not, in any single instance, have been convinced either way. The programs serve only to confuse the listener further; neither the speakers for or against compulsory health insurance seem to know just what they are talking about. Those for the legislation refuse to answer questions designed to point out weaknesses in the bills. Those against the bills protect ineffectually and seldom offer a well informed, specific argument. The only thing of which either side seems to be sure is that it is either "for or agin'." The listener only knows that someone is trying to put something over on him. The tragedy is that he isn't sure just who the villain is.

The bills that have been introduced into the Congress on compulsory

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health insurance are listed as H.R. 345, H.R. 783, and S. 5 and are cited as the "National Health Insurance and Public Health Act of 1949." The bills are identical and are the old Wagner-Murray-Dingell Bill . . . slightly revamped.

The sponsors of the bills claim that they are different from the Medical Act of the British Parliament. I was in England in 1944 when the White Paper on Social Medicine was released, and from study and discussion with British doctors at that time, it is apparent that the two programs are essentially and basically the same. The faults of the British plan for both patient and doctor and the top-heaviness and expense of the Act have been confirmed. The British Act promised, and promises, freedom of practice for doctors and nurses, yet the shortage of doctors and nurses in England increases daily.

To the few patients who were always too poor to get medical aid, the British Act might be considered a benefit. However, because of the avalanche of patients, the service has to be spread so thin that no one benefits. Of what profit is it to a patient to have a diagnosis made if he cannot receive treatment for his disease? The net result of the attempt to treat everyone is that no one is treated.

Not only is there a shortage of doctors and nurses in England, there is a shortage of hospitals, equipment, and medicines. Treatment for those who could be treated is delayed by red tape and regulations. If the patient's complaint is serious, the delay—while he is being sorted out from thousands of patients with minor illnesses—may be fatal.

The sponsors of the compulsory health insurance bills say, "It won't happen here." Remember when the Blue Cross first came into existence? Hospitals were filled with patients with minor complaints—colds and nervous up-sets—and for check-ups; there was no room for the really ill, and valuable time was wasted by doctors and nurses in the routine of admitting and discharging patients who had a "right" to the benefits of the plan. The condition still exists, although to a lesser degree.

To those of us who were in the Army, the memory of red tape and "through channels" is only too vivid. That a good job was done is no credit to the system, but to the availability of inexpensive personnel. The same supply of personnel at the same price could not be obtained unless we became so socialized as to be forced to work for small salaries.

The sponsors of compulsory health insurance deny vehemently that the practice of medicine will come under Federal control. The facts speak otherwise.

The head of the bureau will be a Federal Administrator, the National Health Insurance Board, and an Advisory Council. The Federal Administrator will be a Presidential appointee. The Board will consist of five members, three of whom shall be appointed by the President with the advice and consent of the Senate. The other two shall be the Surgeon General of the Public Health Service and the Commissioner of Social Security.

The Advisory Council shall consist of the *Chairman of the Board* (NHIB) who shall serve as Chairman of the Advisory Council (ex-officio) and sixteen members appointed by the *Federal Security Administrator.* At least EIGHT of the sixteen members shall be individuals who are

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familiar with personal health service and at least SIX of the members shall be individuals who are outstanding in the medical profession or other professions who are concerned with the benefits under this title of personal health service.

A careful analysis shows that the administrative set-up, even in the hands of the wisest and most judicious, is dangerous. In the hands of those who might have other intent, it is dynamite. As a political football, it is perfect. The whole system of medical care immediately becomes a potent weapon in the control of a political situation.

Wherever a state so wishes or can, the plan is to decentralize the administration by delegating it to the states. However, the Federal Administrator and the National Health Board can, at any time, decide it a better policy to assume all of any state administration (see Sec. 241, [e] of [8]). Through channels, the Federal Bureau can take over control of any department, any section, or any person connected with the administration of health services. I don't say that it will, but the bills are so constructed that it can.

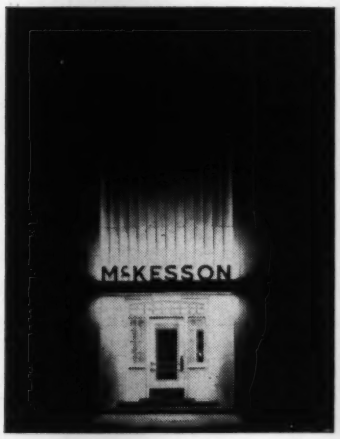
A means of redress is provided for persons receiving or administering health benefit. Under Sec. 262, Par. (B) is found the following: "Provision shall be made for the establishment of necessary and sufficient impartial tribunals to afford hearings to individuals and other persons entitled thereto under sub-section (a) of this section, or section 217 (d) of this title and for further review of findings, conclusions, and recommendations of such tribunals, *in accordance with the regulations made by the Board after consultation with the Advisory Council.* With respect to any complaint involving matters or questions of professional practice or conduct, the hearing body shall contain competent and disinterested professional representation; with respect to any complaint involving only matters or questions of professional practice or conduct, the hearing body shall consist exclusively of such professional persons." (Italics mine.)

The sponsors of the compulsory health bills say that the choice of who shall give medical care to an individual is free—as free as under the present system. I quote Sec. 203 of these bills:

"Every individual eligible for personal health service under this title may freely select the physician, dentist, nurse, medical group, hospital or other persons of his choice to render such services, and may change selection: PROVIDED, That the practitioner, medical group, hospital or other person has agreed under Part B to furnish the class of service required and consents to furnish such services to the individual."

Right here in plain words is the catch: Either the patient must select a doctor, dentist, nurse, medical group, hospital, or other person working under the plan, or pay his own expenses. In this way only does he have absolute freedom of selection. If the sponsors are sincere, they must be expecting all doctors (or others), sooner or later, to enter into the plan or cease the practice of medicine. The situation in England bears this out.

Everyone must, or should, be wondering how this plan is to be financed—this service that the sponsors call "free." No mention of how the funds are to be obtained is made in the bills, other than to say that they will be appropriated. In this connection, I quote Senator Robert A. Taft in an address made at Pittsburgh on February 19, 1949:



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"The bills introduced do not provide any revenue, but it is generally understood that the undertaking will be financed by new taxes amounting to three or four per cent on payroll to be paid by the employees. The tax receipts will have to be supplemented by the equivalent of one or two per cent more in general taxes, so that about four to five billion dollars would come under the control of some bureau of the Federal Security Administration to be dispensed by that bureau to provide free medical service to all the people of the United States, or at least to all those families in which a wage earner has contributed some minimum amount to the payroll tax. The exact manner is not worked out in which medical care will be provided to those who make no contribution, but unquestionably they will also receive free service.

"In the first place this is not a system of insurance at all. The very term compulsory insurance is a contradiction, for insurance is a free act by which a man pays certain definite sums in order to receive protection or benefits worth, according to actuarial computations, approximately what he pays. If he is compelled to pay something to the government, it is a tax, and he has to accept in return exactly what the government gives him. . . . Furthermore the proposed payroll deduction is a tax, because the benefit promised has no relation or a very remote relation to the amount of the payments made. Thus a man with a salary of a thousand dollars and a family of five will pay perhaps $40 a year for services to his entire family, and the man with three thousand dollars a year, but unmarried, pays perhaps $120 for services for himself only. This is the principle of taxation, and not of insurance. The term 'insurance' is used simply because insurance is generally popular, and it is hoped to make the bitter pill more acceptable."

This opinion has not been written without prejudice: one cannot study these bills and the various articles on compulsory health insurance and remain completely open-minded. Except for the discussion of finance, I have touched only those points which seem to have been the source of the greatest contention. The financing of the plans has been little discussed in general because any increase in taxes is a sore subject—at least to Johnny Q. Public.

The single purpose of this review has been to give you a little food for thought on a trend to change the basic structure of your professional lives. S. 1456, the Voluntary Health Insurance Bill, will be discussed at a later date.—VERNA E. BEAN, R.N., Lexington, Ky.

The Journal of the American Association of Nurse Anesthetists

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Relationship of General Nursing and Anesthesia

We have recently observed National Brotherhood Week. For many, it was the same as any other week, except that the word "brotherhood" was mentioned more often on the air and in the press. But more likely than not, our conduct in our daily activities remained unchanged. Perhaps we did let that age-old question arise in our minds: "Am I my brother's keeper?" Or "How much should I do for others? Shall I go about strictly minding my own affairs? How far can I go without having my activities affect someone else?"

If we analyze these questions, we find that we are caught in a web of interrelationships and interactions. We can never be completely independent. This is true in our hospital relationships as well as in our personal lives, for no hospital department is isolated. One is as dependent upon the other as each of us is dependent on each other for food, clothing, and shelter. The interrelationship of general nursing and anesthesia is no exception.

When a patient enters a hospital, he is confident that the hospital is the best, his physician is the best, and his care will be the best, and rightly so. If he is scheduled for an operation, much preliminary work must be done, a large amount of it being general nursing care. A good nurse will see that all orders for tests and treatments are carried out and that all medications are given at the prescribed time. The latter is of special importance to the anesthetist. A poorly prepared patient invites complications under anesthesia, and complications demand more nursing care postoperatively.

Should an unforeseen event take place in the operating room, the anesthetist again leans heavily upon the staff nurse for aid in preparing drugs, blood, plasma, or fluids. This is especially true in small hospitals. And it is a comfort to know that someone is standing by who can be depended upon to act quickly and efficiently.

The vigilance of the general nursing staff the first hours after surgery

again means much to the patient and the anesthetist. It is the staff nurse who can ward off many complications. Although the anesthetist may take credit for giving a good anesthetic, that good anesthetic could come to nought were it not for good postoperative nursing care.

As a good nurse is informed of progress in nursing, medicine, and anesthesia, so a good anesthetist is informed of progress in anesthesia, medicine, and nursing. Neither can give intelligent care without keeping abreast of advances in the interrelated fields.

The interrelationship between general nursing and anesthesia is born of necessity. Yet in many hospitals, the nurse anesthetist is not invited to participate in nursing and hospital activities. Someone has forgotten that she is a nurse who is interested in what goes on about her, even though she is working in a specialized field. The same is true of nurses. As a rule, nurse anesthetists fail to invite the general nursing staff to meetings where advances in anesthesia are discussed. We forget that they might be interested. Yet it would be an advantage to both services and would strengthen the interrelationship of general nursing and anesthesia if, in their meetings, nurses and anesthetists would share their knowledge and become better acquainted.—Marie Kraft, R.N., Madison, Wis.

THE PHYSIOLOGIC EFFECTS OF ANOXIA

Willis G. Watrous, Ph.D., M.D.*
Salt Lake City, Utah

The topic that I am going to discuss with you today has quite extensive ramifications, not only in the field of anesthesia, but widely throughout medicine, and it became a problem of extreme importance for aviators during World War II, as witnessed by the research that was done in high altitude chambers throughout the country. There are extensive sections on the physiologic effects of anoxia in each of the numbers of the *Annual Review of Physiology,* and two significant books have appeared recently, *Anoxia, Its Effect on the Body* by Van Liere,[1] and *Inhalational Therapy* by Barach.[2] Nevertheless, we do not have the time to consider all the effects of oxygen lack, and shall merely consider some of the more important ones as they relate to anesthesia.

Haldane[3] said in 1919 that "Anoxemia not only stops the machine, it wrecks the machinery." As we shall attempt to show, the machine stops in an effort to survive serious anoxemia, and at times the compensatory reflexes are insufficient to prevent transient or permanent damage to the brain or heart. The seriousness of anoxia is illustrated by the fact that man can endure starvation for a maximum of nine to ten weeks, can withstand water or salt deprivation for a few days, depending upon the rate of dehydration, but can tolerate absolute oxygen lack for at most five minutes without irreparable damage to his central nervous system. Accordingly, we as conscientious anesthetists have a special interest in the occurrence, development, and prevention of anoxia. Nevertheless, Mousel[4] wrote two years ago that "Very few anesthesias progress for more than a few minutes in average hands without some degree of anoxia under some of the aforementioned headings (inadequate oxygen in the inspired air, obstructed respiration, respiratory center depression from anesthetic overdose, alveolar membrane edema from anoxia.)" If this is so, it is a wonder to me that human beings are able to withstand the combined insult of anoxia and anesthesia, but perhaps it proves that we are pretty durable.

The motion picture* that you are about to see illustrates the facts you must know concerning the transportation of oxygen in the body and considers the following points: (1) the absorption of oxygen by the blood as it passes through the lungs; (2) the four different types of anoxia and how

Read before the Institute for Nurse Anesthetists, Oakland, Calif., March 8, 1948.

*Formerly with the Veterans Administration in Oakland, Calif.; now with Department of Anesthesiology, University of Utah Medical School, Salt Lake City.

1. Van Liere, E. J.: *Anoxia, Its Effect on the Body* (Chicago: University of Chicago Press, 1942).

2. Barach, Alvan L: *Principles and Practices of Inhalation Therapy* (Philadelphia: J. B. Lippincott Co., 1944).

3. Haldane, J. S.: Symptoms, causes, and prevention of anoxemia and the value of oxygen in its treatment. Brit. M. J. 2:65, July 19, 1919.

4. Mousel, L. H.; Stubbs, D., and Kreiselman, J.: Anesthesia complications and their management, Anesthesiology 7:69-79, Jan. 1946.

**Physiology of Anoxia,* courtesy the Linde Oxygen Company.

each type results in a delivery of less oxygen to the tissues; (3) what happens to the oxygen in the blood after it reaches the tissues; (4) the principles behind the use of oxygen in the treatment of pulmonary edema, pneumonia, cardiac failure, hemorrhage or other forms of anemia, and the poisons such as cyanide, carbon monoxide, and certain anesthetic agents that may interfere with the oxidative enzymes in the tissues. There are two things we need to know first about oxygen before we can fully understand the picture. *First,* the rate at which oxygen is used by the tissues, other factors being constant, depends upon the pressure or tension at which the oxygen is delivered by the blood to the tissues; thus, when the oxygen tension in the lungs is reduced, the oxygen tension in the arterial blood is reduced, and the tension is accordingly reduced in the tissues. The tissues then suffer a depression of metabolism, or resort to emergency, but wasteful and possibly harmful, mechanisms for the production of energy. For example, the brain has no important emergency mechanism and suffers a lowering of metabolism in proportion to the degree of anoxia; however, muscle in the absence of oxygen is able to contract for a while by forming lactic and pyruvic acids. All tissues have to liberate energy continuously merely for the purpose of survival — to maintain cellular structure and organization, for growth and replacement, and to maintain selective permeability of the cellular membranes. Cellular death results when oxidations are diminished below a critical level. The *second* thing we need to know concerns the relationship between the amount of oxygen carried in loose combination by the hemoglobin in the blood and the pressure of the oxygen in the tissues or in the lungs. This is illustrated by the so-called "oxygen dissociation curve of hemoglobin," which shows that, as the pressure or tension of oxygen in the lungs increases, there is a similar increase in the amount of oxygen held by the hemoglobin. The amount of oxyhemoglobin increases rapidly from zero pressure to a pressure which corresponds to about 10 per cent oxygen; further increases in the pressure of the oxygen cause a slower but definite increase in the amount of oxyhemoglobin, until at a concentration somewhere between 14 per cent and probably 20 per cent all of the hemoglobin in the blood is combined with oxygen. In other words, this graph reflects the percentage that blood is saturated with oxygen, hence the name. This curve must be remembered because reflex stimulation of the pulse rate, blood pressure, and respiration bear a close resemblance to this curve until circulatory or respiratory collapse occurs. The oxygen concentration of the air in the lungs is approximately 14 per cent when breathing air at sea level; this corresponds to a tension of approximately 100 mm. Hg, and when in equilibrium or balance with blood, the blood returning to the systemic circulation from the lungs is about 95 per cent saturated with oxygen. The oxygen pressure out in the tissues is much lower, roughly 5 per cent, or 40 mm. Hg; the blood in the tissues quickly loses oxygen until it also has about the same pressure of oxygen as the tissues. The "oxygen-dissociation" graph shows that the blood in doing so gives up 35 per cent of its oxygen, and its new saturation is 60-65 per cent. This blood, which is venous blood, returns to the lungs where it is exposed briefly to a higher pressure of oxygen and is

restored to 95 to 100 per cent saturation.

The problem of anoxia, in the general usage of the term, concerns a deficiency or rarely a lack of oxygen and is closely related to the phenomenon of asphyxia, in which anoxia is associated with an excess of carbon dioxide. The responses of the body to asphyxia are quite similar to those brought about by anoxia, yet there are certain differences that are caused by the toxic action of carbon dioxide. Suffice it to say that oxygen deficiency is more serious and sooner brings about permanent damage to vital organs than carbon dioxide excess, although I do not want to minimize the importance of either anoxia or carbon dioxide excess during anesthesia.

SYMPTOMS AND SIGNS OF OXYGEN WANT

What are some of the symptoms and signs of oxygen want? There may be psychic changes, consisting in overconfidence, impaired judgment and vision, anxiety, dizziness, air hunger, weakness, delirium, and coma. Nausea and vomiting, headache, or precordial (cardiac) pain may be present. Respiratory changes depend upon the severity of anoxia; the rate and depth may be irregular, with the rate tending to increase more than depth, and brief apnea may follow the restoration of oxygen; with more severe anoxia, respiration is first depressed then arrested. The blood pressure shows a slight increase as the pulse rate increases, and as anoxia becomes more severe, the blood pressure may increase acutely, and the pulse may show irregularities, but the latter is often slow, full and bounding; finally, with the onset of cardiac failure, the blood pressure decreases and the pulse ceases. It is said that the pulse increase in the conscious subject is the most reliable index to slight anoxia. Muscular signs largely depend upon the effects of anoxia on the central nervous system; they consist of inco-ordination, twitching, muscle spasms, convulsions, and finally relaxation. The presence of cyanosis generally indicates that anoxia is present, but the depth of cyanosis depends upon the amount of hemoglobin in the blood, the type of skin, and the state of the peripheral circulation. Recent work with the Millikan oximeter[5] showed that some persons are able to perceive a degree of cyanosis corresponding to an oxygen saturation of the blood in the skin of 80 per cent, but the majority of us perceive cyanosis only when the blood contains 5 Gm. of reduced hemoglobin per 100 cc., i.e., when the oxygen saturation is about 65 per cent. Very rapidly produced anoxia, due to the inhalation of undiluted nitrogen, methane, helium, hydrogen, *or nitrous oxide,* will produce coma and unconsciousness with very few warning signs in from forty-five to ninety seconds.

SYMPTOMS AND SIGNS OF CARBON DIOXIDE EXCESS

The patient may experience discomfort with a mild excess of carbon dioxide, or dizziness to unconsciousness with severe excess; the upper part of the respiratory tract tends to be irritated by increased carbon dioxide concentrations. The depth of respiration is markedly increased without much increase in rate in response to mild excesses, but respiration is depressed above a concentration of about 10 per cent and is arrested by a concentration of 30 per cent carbon dioxide. The

5. Comroe, J. H., Jr., and Botelho, S.: The unreliability of cyanosis in the recognition of arterial anoxemia. Am. J. M. Sc. 214: 1, 1947.

blood pressure shows a marked increase but decreases when depressant concentrations are reached; the pulse undergoes a moderate increase. Central nervous system stimulation is shown by twitching, muscle spasm, and convulsions. Henry Hickman[6] showed that carbon dioxide has narcotic properties by producing surgical anesthesia in animals. The skin remains pink owing to vasodilatation unless there is accompanying anoxia. Two types of toxic reactions with severe excess have been described: (1) gasping, depressed respiration, accompanied by pallor, blood pressure decrease, and slow pulse; (2) facial twitchings followed by generalized convulsions with simultaneous failure of the respiration and circulation.

The Systemic Effects of Anoxia

The significant actions of anoxia are confined to three systems, the brain and spinal cord, the respiratory system, and the circulatory system. These three systems are damaged and fail before anoxia can produce functional changes in other organs. The effects of anoxia will be discussed, *first,* without the complicating effect of anesthesia, and *second,* in relationship to anesthesia. The concentrations at which critical changes occur in these functions will be summarized at the end of this discussion.

The circulatory system.—The effects of anoxia may be noted on the blood, on the blood pressure, pulse rate and volume, on the heart, and on capillary permeability. Although prolonged exposure to anoxia may lead to acclimatization, such as occurs at high altitudes or in various circulatory and pulmonary diseases, we are concerned here only with responses to acute anoxia.

The *blood* may show an increase in the amount of blood sugar, as a result of the secretion of adrenalin. There is a reduction of the tension of carbon dioxide in the blood because of respiratory stimulation by anoxia, with a secondary fall in the blood bicarbonate content. With oxygen concentrations of less than 11.8 to 10.6 per cent in the inspired air (remember, the oxygen concentration in the alveolar air is considerably less), there is a slight increase in the blood lactic acid. The main effect concerns the amount of reduced and oxyhemoglobin, as discussed previously; this is significant in regard to the presence or absence of cyanosis, since the blood must have 5 Gm. or more of reduced hemoglobin before cyanosis becomes apparent to most observers. For a person with a normal amount of hemoglobin, this means that an anoxic state equal to breathing approximately 11.4 per cent oxygen or less is necessary, but for a person with anemia the presence of cyanosis indicates a much more severe degree of anoxia.

Capillary permeability increases from various degrees of anoxia, with an increase in the rate of blood flow through tissues and an increase in the rate of formation of both tissue fluid and lymph. This apparently is the mechanism by which active tissues, except the brain, increase their blood flow and supply of nutrients and oxygen. The increase in permeability reaches a maximum with the breathing of 9.8 per cent oxygen in the inspired air. Such an increase would probably have no serious effect on tissues except for the fact that the permeability of the pulmonary capillaries is also increased. In the lungs, the increased tissue fluid that filters

6. Hickman, Henry: Cited by Thompson, C. J. S.: Brit. M. J. 1:843, 1912.

from the pulmonary capillaries may find its way into the alveoli and finer bronchioles, where it interferes with the ventilation of the alveoli and also interferes with the diffusion of oxygen from the alveoli into the pulmonary capillaries. This is one mechanism in the development of pulmonary edema and is the basis for oxygen therapy in pulmonary edema.

The *blood pressure,* like the heart and respiration, is under the control of appropriate centers in the medulla oblongata that are stimulated by carbon dioxide and is also under the control of reflexes that are initiated by the stimulation of sense organs in the carotid bodies and aortic bodies. These structures are stimulated by anoxia. The aortic body is found in the arch of the aorta, and the carotid, where the common carotid arteries divide into the internal and external carotids. These reflexes are truly life saving, for the centers in the medulla are depressed by anoxia, and when these reflexes have been abolished by section of appropriate nerves, mild anoxia may cause sudden collapse, coma, and death. The blood pressure is increased less during anoxia than it is during asphyxia; it shows no sustained increase with oxygen in the inspired air above 11.8 per cent, but below this concentration it may rise 30 to 60 mm. Hg. The increase in blood pressure results from widespread vasoconstriction brought about by the sympathetic nervous system and adrenal glands and serves to divert blood from nonvital organs to the heart and brain. An increase in the pulse rate occurs in all persons breathing less than 14.3 per cent oxygen, and the increase is proportionate to the decrease in oxygen; the increase shows a close correlation to the oxygen-dissociation curve of hemoglobin discussed previously. The cardiac output, which is the amount of blood pumped by the heart in a given time, increases with the breathing of 13 per cent oxygen or less, in the same manner as the pulse rate; the increased output is attributed to the tendency of anoxia to dilate blood vessels. The blood pressure, pulse, and cardiac output increase with decreasing concentrations of oxygen in the inspired air until heart failure occurs; heart failure may occur with the breathing of between 6 and 9 per cent oxygen. Heart failure is accompanied by a rapid decrease in blood pressure, an abrupt decrease in cardiac output, a slowing of the heart rate with onset of various arrhythmias, and an increase in the venous pressure—in other words, the circulation fails when 6 to 9 per cent oxygen is breathed for more than a short time.

The *heart rate* accelerates under anoxia because of the carotid and aortic body reflexes. In addition, anoxia causes the heart to dilate progressively, which means that the heart muscle becomes less efficient. Cardiac failure occurs when the arterial saturation falls to 35 to 50 per cent of normal, which corresponds to an oxygen concentration in the inspired air of approximately 6 to 7 per cent. The coronary vessels dilate under the influence of anoxia; it is believed that the crisis that is announced by cardiac failure occurs as soon as coronary dilatation is unable to keep pace with the decreasing volume of oxygen carried by the blood under various degrees of anoxia. Normal hearts undergo many changes during anoxia that are similar to changes found during disease. Anoxia may cause anginal pains when the coronary arteries are narrowed from disease and may also cause death

from infarction when the coronary vessels are open but narrowed. A severe degree of oxygen lack, near that point at which the heart fails, may cause an intraventricular conduction block, deformation or depression of the QRS complex of the electrocardiogram, flattening or inversion of the T wave, and deviation or depression of the S-T segment. Many of these changes are typical of the effects of coronary infarction in diseased hearts. Irregularities in cardiac rhythm occur only with severe anoxia. It is said that anoxia increases the incidence of cardiac arrhythmias during cyclopropane anesthesia.

The respiratory system. — The lungs provide the means of getting oxygen into and carbon dioxide out of the circulatory system, so that when either system is functioning improperly, all the tissues of the body, including the brain, are subject to anoxia or asphyxia. The regulation of respiration is provided largely by the response of the respiratory center to carbon dioxide and by the reflex responses to anoxia acting upon the carotid and aortic bodies; anoxia primarily depresses the respiratory center. The respiratory stimulation by anoxia is less marked than that by carbon dioxide excess, and the rate of respiration is more affected than the depth. The increase in respiration caused by anoxia is highly variable, some persons showing no effect until unconsciousness is produced; generally, the depth of respiration increases with less than 18 per cent oxygen in the inspired air, while the rate increases with oxygen less than 11.8 per cent. The stimulation continues with increasing anoxia until the depth of breathing abruptly diminishes while the rate increases; this response signals the approach of respiratory failure, which occurs with the breathing of approximately 8 per cent oxygen. Although the deepened respirations help to increase the concentration of oxygen in the lungs, they also serve to wash out carbon dioxide, superimposing hyperventilation upon anoxia, as it were. Certain of the changes that occur in the heart and the brain are caused by the lowering of the carbon dioxide of the blood rather than by the anoxia. The carotid and aortic bodies are not capable of being stimulated by anoxia before birth, so that there is no protective emergency mechanism acting against the harmful effects of anoxia on the fetus; therefore, anoxia of the mother, such as results from nitrous oxide anesthesia when 10 per cent oxygen or less is used, is very likely to cause asphyxia neonatorum.

The brain and spinal cord.— We are most concerned about the influence of anoxia on the central nervous system. Someone said: "Of all the tissues in the body, the nervous tissue is least capable of withstanding oxygen want. In the intact organism, the effect of anoxia on the nervous system is of paramount importance."

In connection with the circulation and respiration, it was noted that the circulation fails with the breathing of a concentration of oxygen between 6 and 9 per cent, and that the respiration fails with the breathing of a concentration of oxygen of about 8 per cent; it should be emphasized that failure does not follow momentary exposure but requires a few minutes. The central nervous system is much more susceptible to anoxia, in that changes in function are noted much sooner. Various subjective symptoms, such as mood change, visual dimness, drowsiness, lassitude, or headache, may be noted with the

breathing of air containing 14.3 to 16.6 per cent oxygen; this corresponds to an altitude of six to ten thousand feet. Changes occur in the electroencephalogram with the breathing of 14 per cent oxygen; impaired co-ordination, with decreased efficiency, memory, and thought, occurs with the breathing of oxygen concentrations between 13.2 and 14.4 per cent. A critical zone has been described and occurs when the oxygen saturation of the blood falls to 80 per cent, occurring with the breathing of oxygen of between 11.4 and 12.8 per cent. At this point there occur beginning neuromuscular changes with tremor or convulsions and exaggerated tendon reflexes, all of which indicate a loss of the inhibitory function of the cerebral cortex; further psychic changes also occur here. Finally, coma occurs in all subjects with the breathing of 9.8 per cent oxygen or less. In relation to nitrous oxide anesthesia, it is of interest that:

Consciousness lasts five minutes or less with the breathing of 7.7 per cent oxygen.

Consciousness lasts ninety seconds with the breathing of 6.4 per cent oxygen.

Consciousness lasts seventy seconds with the breathing of 5.5 per cent oxygen.

Consciousness lasts fifty seconds with the breathing of 4.7 per cent oxygen.

With anoxia, depression of brain functions occurs sooner than permanent damage to the brain cells. Experiments have been performed on animals in which the brain has been deprived of blood for various periods, a state which is comparable with that produced by the breathing of 100 per cent nitrogen or 100 per cent nitrous oxide. The electroencephalographic tracing disappears within fourteen to forty seconds after the onset of this type of anoxia, and the respiratory and circulatory centers are depressed in about the same length of time. However, recovery of the various portions of the brain is possible within different periods of anoxia; when complete functional recovery occurs there is no pathologic damage, and, conversely, impairment or changes in the functions of various brain areas always occur in the presence of pathologic change. The time that is required for recovery of function is proportional to the duration of the preceding anoxia. It has been determined that the small pyramidal cells in the cerebral cortex are the most susceptible to anoxia, and they may show severe damage after total anoxia of but three minutes and ten seconds. Nerve cells in the basal ganglia and in the cortex of the cerebellum are easily damaged by anoxia. Neurons in the medullary centers, while quickly depressed, require exposure to ischemic anoxia for up to twenty to thirty minutes before suffering permanent harm. Cells in the spinal cord and sympathetic ganglia are relatively resistant to anoxia, both with respect to depression of function and the production of pathologic changes.

Nims[7] (1948) emphasized the narrow margin that exists between *reversible* anoxic changes in the central nervous system and *irreversible* destruction of parts of this system.

Although the lower portions of the brain may tolerate considerable periods of anoxia, restoration to normal and survival are limited by the changes that occur in the cerebral cortex and basal ganglia. It is generally agreed that cardiac arrest

7. Nims, L. F.: Respiration. Ann. Rev. Physiol. 8:99-116, 1946.

or respiratory arrest from drowning must be followed by effective resuscitative measures within five minutes after the onset of anoxia.

Relationship Between Anesthesia and Anoxia

The following factors are causes of anoxia during anesthesia: (1) low oxygen concentration in the inhaled atmosphere; (2) obstruction from mucus, tongue, laryngospasm, blood, foreign body, tracheal collapse, etc.; (3) limited tidal exchange due to depression of the respiratory center or to convulsions, pneumothorax, the surgical position, or intercostal paralysis; (4) decreased vital capacity from pulmonary disease; (5) barriers to the diffusion of oxygen, created by such diseases as asthma, emphysema, pulmonary edema; (6) circulatory collapse or failure; (7) interference with tissue metabolic enzymes by the action of certain narcotics.

Anoxic anoxia and anesthesia are most closely associated in regard to the use of nitrous oxide. The two following quotations may be disputed by many. Courville[8] in his classic monograph on *Asphyxia as a Consequence of Nitrous Oxide Anesthesia* said: "Various degrees of anoxia exist and are necessary in the production of nitrous oxide anesthesia, and cellular anoxia strongly reinforces any direct narcotic action of the gas." F. W. Clement[9] in the second edition of his book *Nitrous Oxide-Oxygen Anesthesia* said: "Certain anesthetic gases, as nitrous oxide and ethylene, act primarily by replacing the oxygen of the inspired air. During the narcosis, therefore, both hypoxemia and hypoxia will be present. The degree of oxygen want prevailing at any one time will vary directly with the existing plane or level of anesthesia. . . . The chief concern of the anesthetist is to anticipate from the patient's reactions the evidences of serious or progressive oxygen deficiency, *and to correct the condition before its depressing influence becomes firmly established.*" (Italics mine.)

Accordingly, the Clement-McKesson technic disregards the presence of cyanosis as an indicator of a possible harmful degree of anoxia and bases the need for oxygen upon the respiratory and circulatory responses. A dangerous degree of anoxia is signaled by a progressive decrease in blood pressure with increasing pulse rate and decreased pulse volume, and by an increase in the rate with a decrease in the depth of respiration, which may ultimately lead to periodic or irregular respiration. Dangerous anoxia is confirmed by the oxygen-apnea test, which consists in a breath or two of 50 to 100 per cent oxygen, that is followed by a short period of apnea, then an increased depth of respiration, an increase in the blood pressure, and a slowing of the pulse rate.

Courville[8] and others noted that nitrous oxide has a true narcotic action of its own; therefore, in order to obviate anoxia during nitrous oxide anesthesia, Barach and Rovenstine[10] recommended that nitrous oxide cylinders contain 20 per cent oxygen. With modern technics using such supplementary agents as pentothal, curare, ether, and cyclopropane, it is no longer necessary to combine anoxic depression with nitrous oxide anes-

8. Courville, C. B.: Asphyxia as a consequence of nitrous oxide anesthesia. Medicine 15:129. May 1936.

9. Clement, F. W.: *Nitrous Oxide-Oxygen Anesthesia*, ed. 2 (Philadelphia: Lea and Febiger, 1945).

10. Barach, A. L., and Rovenstine, E. A.: The hazard of anoxia during nitrous oxide anesthesia. Anesthesiology 6:449, Sept. 1945.

thesia in order to achieve easy induction or satisfactory relaxation.

Courville[8] analyzed the data on the anesthesia records for 11 patients who died as a result of nitrous oxide anesthesia and noted that three fourths of them showed respiratory or cardiac failure or both, in a manner indicated by the signs used by Clement and McKesson. Courville believed that asphyxia of the cerebral cortex may occur after the utilization of the small amount of available oxygen in the blood, when transient respiratory or circulatory failure occurs from profound anoxia. Thus, cerebral damage may be done by the time that resuscitation is effective. In the remainder of Courville's cases, there was no respiratory or cardiac crisis; the patient simply failed to rouse at the end of the anesthetic. I believe that this is reason enough to consider it unwise to allow anoxia to continue until cardiac or respiratory signals indicate that the oxygen concentration should be increased.

The damage to the brain caused by anoxia may be widespread, and the changes in function on recovery are legion. Death may occur without recovery of respiration and circulation, or may be delayed a variable period, during which time the patient may show decerebrate rigidity from widespread destruction of the cerebral cortex, or show athetoid movements, convulsions, and other motor phenomena. The patient may survive, but with mental deterioration, symptoms of parkinsonism, blindness, delirium, mania, hysteria, hallucinations, or dementia. It was observed that the chances of resuscitation are better when the respiration rather than the heart fails first.

Anoxia and anesthesia are related to each other in several other ways. There is evidence that some anesthetics, such as chloroform and pentothal sodium, interfere with metabolic enzymes that utilize oxygen for the liberation of energy from glucose by the brain and other tissues. Anoxic anoxia by itself interferes with these metabolic reactions. The anemic person or the person in shock requires considerably less of the anesthetic than a normal person. The technic of "secondary saturation" in nitrous oxide anesthesia involves the superimposition of acute marked anoxia upon a baseline of nitrous oxide anesthesia and may cause profound and prolonged depression. There is evidence from experiments with animals to show that reduction in oxygen tension, reflexly lowering blood pressure, or hemorrhage will increase the prevailing depth of anesthesia. If only for the sake of knowing the depth of anesthesia, it becomes incumbent upon us not to superimpose anoxia upon anesthetized patients. The disorganization of brain function due to anesthesia is sufficiently unphysiologic for further disorganization not to be added to it by anoxia.

There should be positive physiologic evidence, aside from the fact that we customarily breathe 20 per cent oxygen, of the harmful effects of the use of anoxic anesthetic mixtures for more than a very short time. The table shows the altitudes and oxygen concentrations at which significant changes occur in body functions in the unanesthetized state. There is no evidence that anesthesia decreases susceptibility to anoxia, although anesthesia does mask certain normal responses to anoxia.

The brain suffers progressive depression from anoxia, and loss of consciousness occurs with the breathing of 12.8 to 9.0 per cent oxygen. Respiratory movements

ALTITUDES AND OXYGEN CONCENTRATIONS AT WHICH SIGNIFICANT CHANGES OCCUR IN BODILY FUNCTIONS IN THE UNANESTHETIZED STATE

	Altitude ft.	O_2 Concentration %
Cyanosis	16,000	11.4
Acclimatization not possible above	17,500	10.9
Cerebral functions:		
Subjective symptoms of mood change, visual dimness, drowsiness, lassitude, headache, fatigue, increased reaction time, between.	6,000 and 10,000	16.6 and 14.3
Psychic changes with impaired co-ordination, decreased efficiency, memory, thought, between	10,000 and 12,000	14.3 and 13.2
EEG changes begin at	10,000	14.3
**Critical zone,* with loss of mental efficiency, when blood oxygen saturation is 80%, between	13,000 and 16,000	12.8 and 11.4
Cerebrospinal fluid pressure rises from cerebral edema and increased capillary permeability, begins at	14,000 and 15,000	12 or less
Reaction time with choice is markedly lengthened, between	15,000 and 17,000	11.8 and 11.0
Neuromuscular changes with tremor or convulsions, between	15,000 and 19,000	11.8 and 10.6
Exaggerated tendon reflexes, attributed to a decrease in function of the cerebral cortex, between	15,000 and 29,000	11.8 and 6.7
**Coma* occurs in the unacclimatized at altitudes between	20,000 and 22,500	9.8 and 8.9

Circulatory functions:		
Pulse increase, closely follows the oxygen dissociation curve, usually occurs above.....	10,000	14.3
Cardiac output is significantly increased when blood oxygen saturation falls to 82%, at.....	13,000 and 14,000	12.5
Blood pressure shows sustained rise above	15,000	11.8
Lactic and pyruvic acids in blood rise at altitudes of.....	15,000 and 18,000	11.8 and 10.6
Capillary permeability increase from anoxia, maximum at.....	20,000	9.8
**Cardiac crisis* occurs when the blood oxygen saturation falls to 35-50%, with a fall in blood pressure and rise in venous pressure from heart failure; arrhythmias, flat T-wave, conduction disturbances, including intraventricular block, occur at.....	30,000	6 and 7
Respiratory functions:		
Respiratory crisis may occur in the absence of chemoreceptor control at	10,500	14
Respiratory stimulation becomes significant at 15,000 feet, then follows oxygen dissociation curve	15,000	11.8
**Respiratory failure* occurs at....	25,000	8

*Indicates critical oxygen concentrations for cerebral, cardiac, or respiratory functions.

fail on 8 per cent oxygen, and cardiac crisis occurs with 6 to 7 per cent oxygen in inspired air.

Special surgical conditions may produce anoxia insofar as they interfere with adequate respiration: operations on the heart and lung when the chest wall is opened; the prone position; the lateral position, particularly with use of the kidney lift; a steep Trendelenburg position with laparotomy packs.

One subject remains to be considered, and that is the influence of the anesthetic agent upon the reflexes initiated by the action of anoxia on the carotid and aortic bodies. In some cases these responses are markedly altered or depressed, so that the reflex responses to anoxia may be weakened or absent. *Nitrous oxide* and *ethylene* apparently have little or no effect on these reflexes. *Diethyl ether* depresses the responses of the carotid bodies to anoxia, the respiratory response being less affected than the blood pressure reflexes; the pressor effect of anoxia may be lost during deep ether anesthesia. *Chloroform* abolishes the responses, both respiratory and circulatory, of the carotid body to anoxia. *Evipal* and *pentothal sodium* tend to exaggerate the respiratory and circulatory responses to anoxia during anesthesia of moderate depth, but the respiratory responses are abolished by deep anesthesia, while the blood pressure responses are preserved; in animals the respiratory responses are preserved in deep anesthesia as well. The administration of oxygen during deep pentothal sodium anesthesia may cause "oxygen apnea." *Cyclopropane* depresses all the responses initiated by anoxic chemoreceptor stimulation. *Morphine* tends to exaggerate the responses, both respiratory and circulatory, of the carotid body to anoxia.

SUMMARY AND CONCLUSIONS

Although the human body is somewhat tolerant to mild degrees of anoxia, it may be difficult, particularly in a patient under anesthesia, to ascertain the existence of under-oxygenation by changes in the blood or by reflexes, except by use of blood-oxygen determinations or by the Millikan oximeter. Because of the risks of permanent cerebral or cardiac damage, the use of anoxic gas mixtures is not justified. The use of anoxic mixtures of nitrous oxide or ethylene to facilitate induction or relaxation is not justified in the light of present day usage of adequate premedication and balanced or combined anesthesia. Either anoxia *or* anesthesia is capable of depressing the psychic and vital functions of the brain and the effectiveness of the circulatory and respiratory systems. Anoxia *and* anesthesia have additive effects that are cumulative.

SOME PHYSIOLOGIC RESPONSES AFFECTING ANESTHESIA

Morgan L. Allison, D.D.S.*
Columbus, Ohio

This article is primarily a review of physiologic conditions and responses that may be influenced by anesthetic agents and that may influence the choice of the anesthetic agent used. The administration of every anesthetic is an experiment in human physiology. The anesthetist is the only person permitted to do human experimentation as a routine part of his work. Each anesthetic administered is a different problem in physiology, and every anesthetic is a major procedure regardless of the length of time of anesthesia, the general condition of the patient, and the surgical procedure. For these reasons we always observe and appraise the responses of the patient to the anesthetic agents, fluids, and drugs administered, oxygenation of the blood, and removal of carbon dioxide from the system.

under normal circumstances is regulated by carbon dioxide tension. The number of molecules of carbon dioxide within each cell of the respiratory center determines the activity of the center, and this number is determined by the carbon dioxide tension of the blood. Carbon dioxide in small doses or a slight increase in the carbon dioxide tension of the blood is stimulating to the respiratory center and thus stimulates respiration. An increase of 0.3 volumes per cent of carbon dioxide in the blood will often double alveolar ventilation, whereas a similar decrease of carbon dioxide in inspired air may be followed by apnea.[1-3] On the average anesthetic machine with the usual soda lime method for removal of carbon dioxide and under optimal conditions, the carbon dioxide concentration in the inspired air is 0.1 per cent to 0.3 per cent. Therefore, the respiration of the patient will be stimulated depending on the individual, the preoperative medication, the depth of anesthesia, and the efficiency of the carbon dioxide absorbing agent.

RESPIRATION AND RESPIRATORY REFLEXES

Respiration and the respiratory reflexes are the most important physiologic signs used during anesthesia. Inspiration normally is active, produced by contraction of the diaphragm and the intercostal muscles; expiration normally is passive, owing to relaxation of inspiratory muscles and collapse of the chest wall. The control of respiration

Abnormal conditions frequently are present during anesthesia, and they may affect respiration. Hypoxia always depresses the respiratory center, but it may increase respiration by reflex stimulation of the

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*Department of Anesthesia, Ohio State University.

1. Schmidt, C. F., and Comroe, J. H.: The functions of the carotid and aortic bodies. Physiol. Rev. 20:115, 1940.
2. Bard, P.: *MacLeod's Physiology in Modern Medicine*, ed. 9 (St. Louis: C. V. Mosby Co., 1941) pp. 564, 575, 584, 664.
3. Best, C. H., and Taylor, N. B.: *Physiological Basis of Medical Practice*, ed. 4 (Baltimore: Williams & Wilkins Co., 1945) pp. 346, 349.

chemoreceptors in the carotid body. In severe hypoxia, regulation of respiration will be taken over by the chemoreceptors, mainly those in the carotid body. The chemoreceptors are not affected by the presence of normal blood oxygen tensions, but they do not regulate respiration under such conditions. They are stimulated by hypoxia or low blood oxygen tensions.

In severe hypoxia the respiratory center is depressed, and the chemoreceptors regulate respiration. Under such conditions, if a breath of pure oxygen is given, the patient may stop breathing. This is oxygen apnea.[4-7] The breath of oxygen will increase blood oxygen tensions sufficiently to remove the stimulus to the chemoreceptors, and yet it is not sufficient to relieve the depression of the respiratory center. Also, the carbon dioxide tension of the blood may be lowered sufficiently to be ineffective as a stimulus to respiration. The patient will not breathe voluntarily until the respiratory center depression is overcome and the blood carbon dioxide tension is increased. It is necessary to maintain artificial respiration or controlled respiration by positive pressure with oxygen until these conditions are established. This situation occurs most often after nitrous oxide-oxygen anesthesia using high percentages of nitrous oxide. It may also occur after hypoxia caused by respiratory tract obstruction, although in such a case the blood carbon dioxide tension is not lowered. Under the same conditions, the pressoreceptors in the carotid sinus are highly excitable. Any severe stimulation of these receptors, by direct trauma or by pressure exerted by the anesthetist in attempting to hold the tongue forward by pressure on the angle of the mandible, may cause a reflex drop in blood pressure. This will increase the anoxia of the brain and the heart, and such serious depression may occur as to cause irreversible changes in the patient's condition.[8, 9]

Cyanosis is not a measure of anoxia. Cyanosis is a color. A patient will be cyanotic when he has 5 Gm. unoxygenated hemoglobin per 100 cc. blood.

In polycythemia, the patient may be cyanotic and yet adequately oxygenated with sufficient blood oxygen tensions. The anemic patient may never become cyanotic, and yet he may suffer from an insufficient supply of oxygen to the tissues. This is because he cannot have 5 Gm. reduced hemoglobin per 100 cc. blood.

Severe pain and generalized excitement may cause hyperpnea, which if prolonged will result in hypocapnia. Sudden relief from pain by an anesthetic may result in apnea, since the respiratory stimulus of carbon dioxide has been removed by the hyperpnea. Such a condition most often will occur in children or excitable adults after severe trauma or apprehension. A child may come to the operating room struggling and screaming and in a state of excitement with rapid and deep breathing so that he is hyperventilated and the blood level of carbon dioxide is very low. When an anesthetic is administered to such a patient, the stimulus (pain or excitement) for respiration is removed. The normal stimulus for

4. Van Liere, E. J.: *Anoxia, Its Effect on the Body* (Chicago: University of Chicago Press, 1942) pp. 107, 109.
5. Bard, P.: op. cit., p. 584.
6. Schmidt, C. F., and Comroe, J. H.: Science 92:510, 1940.
7. Schmidt, C. F.: Functions of the carotid and aortic bodies. J. Lab. & Clin. Med. 26:223, 1940.
8. Bard, P.: op. cit., pp. 664, 665.
9. Goodman, L., and Gillman, A.: *Pharmacological Basis of Therapeutics* (New York: The Macmillan Co., 1947) p. 86.

respiration is missing because the patient has hyperventilated and lowered his blood carbon dioxide tension, removing the stimulus. Such a situation may also occur in the emergency room when a child is brought in after a painful accident. Before an anesthetic is administered to such a patient, it is important to have a means of administering oxygen with artificial respiration immediately available. This apnea is self limiting and will be overcome. Apnea is particularly dangerous in patients with cardiac disease who cannot tolerate any degree of hypoxia. Precautions should be taken before administering pentothal sodium to such a patient, because the state of excitement may cause the patient to require a larger amount of the drug than usual. Then, when the pain or apprehension is removed, the blood concentration of the drug may be sufficient to cause prolonged respiratory depression and apnea.

Coughing is a protective mechanism by which the body is able to expel foreign material from the trachea. The vocal cords are held together tightly, and the intrathoracic pressure is increased tremendously. Suddenly the cords open, and the air in the lungs is expelled with explosive violence. Under anesthesia the cough reflex is changed to breath-holding or deep active expirations. This helps to counteract respiratory depression of the central nervous system. Under deep anesthesia direct irritation of the respiratory passage, e.g., with ether, may keep the patient breathing. A change to a nonirritating anesthetic agent will remove this stimulus and may cause apnea that will be fatal if artificial administration of oxygen is not begun.[10]

10. Bard, P.: op. cit., p. 599.

The cough reflex disappears under anesthesia, first in the upper respiratory passages and last, under very deep anesthesia, in the lowest portion of the respiratory passages. Because of this, a patient may be in surgical anesthesia and well relaxed, yet he will cough when an intratracheal tube is inserted because of the stimulus to the trachea where reflex irritability has not disappeared. Such stimulation often changes a smooth anesthetic procedure into a struggle between the patient and the anesthetist that may end only when the patient is fully conscious. Cocaine, 4-10 per cent, or pontocaine, 2 per cent, sprayed on the vocal cords and into the trachea under direct vision with laryngoscopy a minute before the tube is inserted will anesthetize the mucous membrance of the passage and will reduce reflex irritability and prevent coughing and biting by the patient. After the tube is inserted, if the patient is in the first plane of anesthesia and bites down, an oropharyngeal airway should be placed in his mouth before the blade of the laryngoscope is removed. This prevents obstruction of the airway by closing the lumen in the tracheal tube.

As mentioned before, the cough reflex is a protective mechanism. The normal cough reflex disappears in the second plane of third stage anesthesia. However, if a catheter is passed down the trachea, it will still produce coughing. The deeper it is passed into the respiratory passages, the stronger the cough becomes. It will bring up secretions from deep within the lungs and will make it possible to pick up such material with the catheter that otherwise would not be reached. The use of topical anesthesia on the cords as previously described will not remove this reflex.

There are other stimuli which may cause coughing during anesthesia, including scraping of the periosteum during rib resection and dilation of sphincters.

Bronchiolar spasm may occur during anesthesia. It is always a difficult problem and is dangerous if not recognized. It does occur because of allergy, and it may occur after the administration of cyclopropane or curare. It is identified by maintaining an open airway into the trachea and then by the pressure required to inflate the lungs. Once it has been identified, the treatment is oxygen under pressure or oxygen-helium mixtures under pressure. Cyclopropane and curare should be discontinued.[11]

Laryngospasm is a prolonged contraction of the vocal cords. It occurs during light anesthesia and is caused by irritation of the mucous membrane of the respiratory passages and vocal cords. High concentrations of anesthetic agents, pharyngeal airways, the tongue touching the pharyngeal walls, and blood, mucus, or foreign bodies may cause it. Laryngospasm may also be caused by reflexes during traction on the mesentery, dilating of sphincters, stripping of periosteum, or any severe manipulation. The treatment is to remove the cause and to administer oxygen under pressure. Oxygen-helium mixtures may pass the cords easier than oxygen alone. Atropine given intravenously or curare sometimes is effective in breaking up laryngospasm. Atropine may be given intravenously in doses of grain 1/50 to 1/75 and repeated if necessary. Pentothal sodium does not cause laryngospasm but may predispose to it. The laryngeal reflexes are not abolished; in fact, they may become hyperactive. If mucus, vomitus, or another foreign body touches the larynx, spasm may result. Irritating ether vapor may have the same effect.

Breath-holding occurs during light anesthesia when the patient objects to the inhalation agent or suffers pain from trauma or manipulation. It occurs during anesthesia of moderate depth from such stimuli as stripping the periosteum, tugging on the mesentery, puncturing the pleura in thoracic surgery, and dilating sphincters. It will end when the stimulus is removed or when the depth of anesthesia is increased.

Dyspnea is the sensation of difficult breathing with a conscious effort to ventilate the lungs. There are many causes, but any dyspneic patient is a poor risk for general anesthesia. Dyspnea in patients with cardiac disease usually is due to their inability to increase the depth of respiration and corresponds to a diminished vital capacity. The closer the tidal volume approaches the vital capacity, the more dyspneic the patient becomes. More will be said of dyspnea when the heart is discussed.

Pneumothorax is the condition in which the pleural space communicates with the air. It can be accidental or surgical. Pneumothorax removes the normal negative pressure of the chest, allows the lung to collapse, and allows the mediastinum to move toward the opposite side. During thoracic surgery these conditions will occur if precaution is not taken to prevent them. The shift of the mediastinum to the closed side reduces vital capacity, causes torsion of the large vessels, and places the heart in an abnormal position. The mediastinum will

11. Lundy, J. S.: *Clinical Anesthesia* (Philadelphia: W. B. Saunders Co., 1942) pp. 441, 451.

change position with each respiration, and this may lead to heart failure.

Paradoxical respiration may occur when pneumothorax is present. During inspiration, air is drawn from the lung on the open side into the lung on the closed side; during expiration the reverse occurs. The exchange of gas between the lungs and the atmosphere is diminished, and anoxia and hypercapnia may result.

The treatment for paradoxical breathing and mediastinal shift is positive pressure. There are two schools of thought on the effects of pulmonary positive pressure. One is that 8 mm./Hg pressure is necessary to maintain the oxygen tension of the blood and to prevent mediastinal shift and paradoxial breathing. The other group believes that 8 mm./Hg pressure will reduce venous return and cardiac output and that cardiac failure may follow. The amount of positive pressure necessary to satisfy both conditions is the amount of pressure necessary to expand the lungs sufficiently to prevent mediastinal shift and paradoxial breathing and to provide satisfactory blood oxygen tensions. This amount of pressure is determined by observing the lung expansion and mediastinal movement, the pulse rate and blood pressure changes, and the color of the patient.

Pneumothorax diminishes reserve air and reduces the tidal volume. It also interferes with venous return because of the loss of the pumping action of negative intrathoracic pressure. Closure of a thoracic opening should be made at the end of expiration so that the intrathoracic pressure will be subatmospheric on inspiration and assure expansion of the lung.

Tension pneumothorax occurs when there is a valvelike opening into the chest so that air can enter the chest on inspiration but cannot escape on expiration. Collapse of the lung on the affected side is followed by increased intrathoracic pressure on this side. This pushes the mediastinum to the unaffected side, and the lung on the unaffected side will be compressed. This condition may lead rapidly to a fatality. Such a wound requires immediate treatment: A large gage needle should be inserted into the pleural cavity on the affected side. A rubber finger cot is tied over the hub of the needle and the tip cut from the finger. This will permit air to come out of the chest through the needle on expiration, but it will prevent air from entering the chest through the needle on inspiration. This will prevent an increase in intrathoracic pressure until the condition can be corrected by surgery.

Tension pneumothorax can result from closure of the chest wall after surgery or from a perforation of lung tissue during surgery. The latter condition is not so easily diagnosed. The lung tissue acts as a valve admitting air into the pleural space on inspiration. On expiration the opening collapses and prevents the escape of air from the pleura. In this manner tension pneumothorax occurs from inside the chest, and anoxia develops. Immediate treatment is the same as that previously described.

In thoracic or upper abdominal surgery when the pleura is punctured either intentionally or accidentally, the patient may hold his breath or cough even though he is in deep anesthesia. It may also cause cardiac slowing and a decrease in blood pressure. These changes are self limiting and will

usually correct themselves when the stimulus has passed.

A rise in body temperature increases body metabolism and the oxygen demand of the tissues. There is a 7 per cent increase in metabolic rate for every degree of temperature increase. This is most important when open drop ether or nitrous oxide-oxygen is used.[12] In such instances, the oxygen content of the inspired air should be increased. With the open drop system, oxygen insufflation should be used. Except in experienced hands, nitrous oxide-oxygen is contraindicated as the primary anesthetic for patients with a high metabolic rate.

Circulation and Circulatory Reflexes

In addition to respiration, the circulatory system and its reflexes are of importance to the anesthetist. The pulmonary and portal systems are not easily observable, and the peripheral circulatory system is our principal concern. Blood pressure and pulse pressure and the rate, rhythm, and quality of the pulse are the main signs of the condition of the circulation. Arterial blood pressure is modified by many factors, the principal ones being the rate of the heart, stroke volume of the heart, and the peripheral resistance. Inspiration is accompanied by a negative intrapleural pressure and increases the venous return to the heart. The respiratory movements act as an accessory heart.

Nervous control of the blood vessels is both sympathetic and parasympathetic. Parasympathetic impulses cause constriction of the coronary vessels, while sympathetic impulses cause constriction of peripheral vessels. It is important that the correct drug be used for vasopressor action, because constriction of the coronary vessels of patients with cardiac disease and constriction of the coronary vessels of any patient with anoxia may be fatal.

The blood pressure is normally regulated from the vasomotor center through reflexes from pressoreceptors (and chemoreceptors to a lesser extent) in the carotid sinus and the aortic arch. The center is also influenced by changes from normal carbon dioxide and oxygen tensions of the blood and pH, as well as heat and cold, pain, emotion, and drugs, including anesthetic agents.

The control of heart rate is normally a balance between sympthetic and parasympathetic influences. The first five thoracic sympathetic nerves are cardiac accelerators; the vagus nerve is parasympathetic and slows heart rate.

There are many influences on blood pressure and heart action during anesthesia. Spinal anesthesia causes relaxation of the vessels of the parts anesthetized and will cause a decrease in blood pressure by lessening peripheral resistance and venous return. If the level of spinal anesthesia is high enough to affect the upper five thoracic sympathetic nerves, the cardiac accelerating action is lost, and the heart rate slows because the influence of the vagus now predominates. Sympathectomy removes the constricting influence of the sympathetic fibers on the blood vessels they supply. This causes a decrease in blood pressure, and during second stage sympathectomy the decrease may be severe.

During chest surgery when there is manipulation of the hilus of the lung and during vagotomy when

12. Best, C. A., and Taylor, N. B.: op. cit., p. 321.

the nerves are sectioned, the vagus stimulation may be so severe as to cause partial or complete heart block. This may be prevented by injection of procaine into the hilus or around the vagus before manipulation or the cutting of the vagus. If procaine is not used, atropine given intravenously will lessen vagal influences and prevent slowing of the heart rate. An intravenous infusion of 0.1 per cent procaine is also useful.

Venous return of blood to the heart is important to the anesthetist. There are two factors that determine venous return. The first is venopressor action through chemical, thermal, or nerve reflexes. The second is pressure gradients, which are affected by the pressor action just described, reduced central venous pressure on inspiration, valves in the veins, muscular contractions, and gravity. The gravity influence of a 15 degree Trendelenburg position will move 500 cc. of blood to the thorax and head areas. During shock, this helps to maintain the blood volumes in the vital centers of the heart and brain at the expense of the less important and more resistant lower extremities. A weak heart may be overburdened by an increase in venous return with decompensation during anesthesia.

Cardiac decompensation occurs when the heart is unable to expel the blood returned by the veins. Clinical signs of heart failure are dyspnea, orthopnea, and edema. In left ventricular heart failure, the heart is unable to expel the blood flowing to it from the pulmonary system. This causes congestion of the blood vessels of the lungs and pulmonary edema with dyspnea, the important clinical signs of left ventricular heart failure.

In right heart failure or decompensation, the volume of blood delivered to the pulmonary system is reduced, and the output of the left heart may equal the volume delivered through the pulmonary system. The congestion of the lungs is relieved, and the patient's dyspnea improves or disappears. However, the blood accumulates in the veins behind the right heart, and edema, ascites, and enlarged liver appear. These are the clinical signs of right heart failure. The patient may look better and feel more comfortable because the dyspnea has improved, but his heart is in a more serious condition than before. These signs should be observed and understood by the anesthetist before he gives such a patient an anesthetic. Compensatory factors involved in heart failure include cardiac dilatation and hypertrophy.

Systolic blood pressure is measured by the transmission of a pressure wave along the arterial wall following the systolic ejection of blood from the left heart. Diastolic pressure is caused by the pressure exerted by the elastic tension of the vessels and peripheral resistance. Pulse pressure is the difference between systolic and diastolic pressure.

Changes in any of these pressures during anesthesia should be observed and their causes determined when possible. Changes in pulse pressures occur when there are discordant changes in systolic and diastolic pressures. For instance, an increase in peripheral resistance or an increase in heart rate will cause an increase in both systolic and diastolic pressure, but the diastolic pressure will usually increase more than the systolic so that there is a decrease in pulse pressure. An increase in systolic discharge causes

an increase in both systolic and diastolic pressures, but the systolic pressure increase is greater than the diastolic so that the pulse pressure is increased. An increase in aortic volume is associated with a relative decrease in systolic discharge. Therefore, systolic pressure decrease is greater than diastolic pressure decrease, and the pulse pressure will be decreased. A decrease in arterial distensibility is followed by an increase in systolic pressure, a decrease in diastolic pressure, and an increase in pulse pressure.

During systole there is little blood flow through the coronary arteries. It has been said that the nutrition of the heart takes place during diastole. The aortic diastolic pressure forces blood through the coronary arteries while the heart muscle is relaxed and the vessels can be filled easily. Therefore, any significant drop in diastolic pressure is dangerous, especially in patients with hypertensive or cardiac disease.

Heart block is a defect in the conduction of an impulse from the auricle to the ventricle. The rhythm of the heart is regulated by impulses that arise in the sino-auricular node and spread across the auricles and through the ventricles. Trauma, infection, or the loss of blood supply to Purkinje's fibers of conduction will cause heart block. It is because of this last factor that diastolic pressure should be maintained during anesthesia. It is just as important to prevent an excitement state, prevent overburdening of the heart, and maintain blood oxygen tensions.

Summary

The purpose of this article has been to outline some of the more important physiologic reactions of the respiratory and circulatory systems that should be of interest to the anesthetist. It is hoped that it may serve as a stimulus for further study and clinical research in physiology during the routine management of anesthesia.

RESPIRATORY AND CARDIAC EMERGENCIES DURING ANESTHESIA

Larry Schull, M.D.*
Nashville, Tenn.

I appreciate your kind invitation to address this gathering. These meetings should help foster the good feeling between the nurse anesthetist and the anesthesiologist that some individuals on both sides seem intent on destroying. Much remains to be achieved in the field of anesthesia, and the rate of advancement depends on sincere co-operation among us all. In this discussion certain conditions will be reviewed that we have all observed, and some suggestions for treatment will be presented.

RESPIRATORY TRACT OBSTRUCTION

The most common respiratory emergency is simple upper respiratory tract obstruction. Most of us are so sensitive to its occurrence that we can sit in an office on the surgical floor and identify a patient with obstruction fifty feet down the hall. One of the most annoying types of simple obstruction is the type usually encountered in the patient with a short neck and heavy jowls. The minute the patient loses consciousness, the tongue falls into the oropharynx, and the anesthesia is too light to insert an oral airway. It naturally follows that the induction of anesthesia in such a patient is prolonged. Adequate respiratory exchange may be obtained by inserting a well lubricated, no. 6 intratracheal tube that has been cut in half through the nose and into the oropharynx. This procedure is also effective for a patient who does not have adequate respiratory exchange with an oral airway and is too lightly anesthetized for tracheal intubation.

The nasal route of intubation is also effective for the patient who is not relaxed enough for oral intubation. Every anesthetist has had a patient who vomited during the course of pentothal sodium anesthesia, for example, and whose jaws were clamped together. The insertion of a nasal intratracheal tube enables the anesthetist to clear the bronchial tree without having to wait while the anesthesia is deepened.

The presence of mucus and blood in the nasopharynx is, unfortunately, too familiar to all of us. The condition frequently causes pronounced respiratory tract obstruction. This type of obstruction occurs in several types of cases. It occurs when there is a hypersecretion of mucus in a child who has not had atropine in adequate amounts. The best means of coping with this situation is the judicious prophylactic use of atropine. I believe that far more children are harmed by partial obstruction from mucus than from the administration of atropine. If excessive amounts of mucus are present, the use of a suction catheter and suction tip is effective in keeping the pharynx clear. This type of obstruction may also occur in the patient undergoing tonsillectomy and adenoidec-

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*Clinical Instructor in Anesthesia, Vanderbilt Medical School.

tomy. The assistant often cannot, in addition to his other duties, keep blood out of the lower pharynx and trachea. In this type of patient we perform pharyngeal and tracheal suction under direct vision with the laryngoscope at the end of the procedure. In each and every case we get some bloody debris from the trachea. When the patient is an older child or an adult, the operation is performed under intratracheal anesthesia, and the airway is easily kept clear.

In this category is a type of patient seen occasionally in civilian life and commonly during wartime, that is, the patient with a maxillofacial injury. If the operation is performed under general anesthesia, it is imperative that the patient have an intratracheal tube in place to enable the anesthetist to keep the respiratory passages clear. Intubation may be done under local anesthesia prior to the induction of general anesthesia, or curare may be used with pentothal sodium as the anesthetic agent.

The larynx is the most important structure in the respiratory tract from the standpoint of both smooth anesthesia and the safety of the patient. The direct cause of laryngospasm is parasympathetic stimulation. This stimulation results from mucus around the larynx, traction on viscera during light anesthesia, incisions during light anesthesia, or too large a concentration of the anesthetic agent, especially ether.

Two anesthetic agents predispose to the occurrence of laryngospasm. These are pentothal sodium and cyclopropane. Accordingly, one must be constantly on the alert for the occurrence of laryngospasm when these agents are used. The degree of spasm varies from noisy stridor to complete occlusion. In the presence of any degree of laryngospasm, the respiratory tract is partially obstructed. A mild degree of spasm will interfere with the exchange of gases and prolong the induction period. With an increase in the severity of the spasm, the patient shows increased evidence of anoxia and carbon dioxide retention, which in itself increases the spasm. The presence of either of these conditions for any length of time is detrimental to the patient.

The treatment of laryngospasm varies with the cause, and frequently several corrective measures are necessary. The surgeon should stop operating until the anesthesia can be deepened. When pentothal sodium is being used, more of the drug should be given to deepen the anesthesia, and the bag pressure should be increased to force more oxygen through the cords. If the spasm persists, curare may be used to relax the cords. If the spasm is due to too high a concentration of ether, the bag mixture should be diluted.

Should the spasm persist after these measures have been taken, intratracheal intubation should be performed. When the spasm is too pronounced for intubation, a tracheotomy may have to be done. The use of an intratracheal tube makes it possible to maintain anesthesia at a lighter plane than would be possible without the tube, since one does not have to deal with spasm. Frequently there will be moderate laryngospasm on extubation; this is transitory, however, and no treatment is necessary.

Obstruction of the lower respiratory tract may be one of several types. Obstruction from blood and mucus has already been mentioned. Not only does such obstruction interfere with physiologic functions, but it makes maintenance of the

anesthesia difficult. The best means of combating this complication is the use of the intratracheal tube and of tracheal suction. The greatest need for intratracheal anesthesia is in thoracic surgery, especially for the patient having suppurative disease of the chest, lung abscess, or bronchiectasis. This type of patient has excessive drainage into the bronchial tree, and constant bronchial suction is required. I have seen patients who were almost impossible to keep asleep because of the need for bronchial suction. I have also seen sudden rupture of an abscess with the spilling of 100-200 cc. of foul exudate into the bronchus. If an intratracheal tube had not been in place, the patient would have drowned in his own exudate.

In an operation on a patient with pulmonary tuberculosis, it is almost obligatory to have an intratracheal tube in place so the trachea may be kept clear and spread of the disease to an uninvolved portion of the lung prevented.

The prompt recognition of these conditions will enable the anesthetist to prevent the occurrence of a death, postoperative atelectasis, or the spread of a debilitating disease.

When vomitus is aspirated, although it may be necessary to perform bronchoscopy, the anesthetist may clear the bronchi by tracheal suction, with or without a tube. We endeavor to have the bronchial tree of a child dry before he is returned to the ward; we nearly always perform tracheal suction on children.

Another type of bronchial obstruction results from bronchial spasm. The condition is characterized by fixation of the chest in expiration, difficulty in expanding the chest even with positive pressure, and a patent airway. Mild obstruction may be identified by the wheezes and squeaks characteristic of asthma. A case report is illustrative:

A man, aged 55, had a typical asthmatic attack during thoracolumbar sympathectomy. The patient gave no history of previous attacks. The attack was controlled with ephedrine given intravenously. Prior to the second stage of the operation, he was given pyribenzamine and aminophylline intravenously. During this procedure he had no difficulty.

Bronchiospasm is seen occasionally during pentothal sodium anesthesia and also when curare is used. It has been clinically demonstrated that curare causes the release of histamine in the body with resultant allergic effects.

A man, aged 35, was admitted for tendon repair. Prior to the incision, laryngospasm developed. The patient was given 60 units of curare intravenously with improvement. In about two minutes, however, he was again having no respiratory exchange. Upon laryngoscopy his cords were found to be in complete spasm, and it was impossible to insert an intratracheal tube. A tracheotomy was done, and artificial respiration was attempted, but it was not possible to inflate his lungs. He was given 50 mg. ephedrine intravenously with immediate relaxation of the spasm, and respiration was again possible.

When curare is used, bronchiospasm is more common if the patient is awake. In treating tetanus with curare, one must be especially vigilant for the occurrence of bronchiospasm and have ephedrine as well as prostigmine on hand.

RESPIRATORY IRREGULARITIES

Respiratory irregularities are often the source of great concern to the anesthetist. Such irregularities occur most frequently in thoracic surgery and neurosurgery. When apnea occurs for any reason, the anesthetist should take immediate steps to ascertain the cause. We are all familiar with the occurrence of hyperventilation during induction or maintenance of anesthesia followed by a period of

apnea. The cause, of course, is the elimination of carbon dioxide. During this type of apnea the patient's color is pink, and respiration begins spontaneously.

In thoracic surgery the irregularities usually begin with the stripping of the periosteum. In nearly every patient I have seen, this procedure results in a short period of apnea that ends as soon as the procedure is completed. When the chest is opened, respiration becomes labored, and there may be some cyanosis. The use of positive pressure anesthesia frequently corrects the condition, and the patient will tolerate the open chest well. An occasional patient will not have adequate respiratory exchange even with the use of positive pressure, and reinforced respirations by gentle bag pressure to aid aeration are indicated. In some cases it may be necessary to take over the respiration completely and give controlled respiration.

When the surgeon is dissecting tissue around the hilus, breath-holding is common and is usually corrected by deepening the anesthesia. Most of these irregularities are self limited, and the color remains good.

During neurosurgical procedures one may expect all sorts of aberrations in respiration from the beginning of the induction. The patient having increased intracranial pressure presents the most serious problem. Such a patient will occasionally begin to have Cheyne-Stokes respiration as soon as the anesthesia is started. There is nothing to be done for this condition. The irregularity may disappear when the cranium is opened and the increased intracranial pressure relieved. When the operative procedure is in the region of the cerebellum and third ventricle, any sort of respiratory irregularity may be expected; such irregularities are due to traction on the medulla. The anesthetist should be prepared to assist the respiration at any time by having an intratracheal tube in place. This preparation enables the surgeon to proceed with the operation with a minimum of disturbance. The patient may suddenly stop breathing at the end of the operation although the pulse remains strong; here again it is necessary to give artificial respiration until a ventricular needle can be inserted and fluid removed. In addition it may be necessary to place the patient in a respirator to return him to his room. After such a procedure an intratracheal tube should not be left in place for longer than four or five hours, since laryngeal edema will result.

Even when regional anesthesia is used, respiratory difficulty may occur. During spinal anesthesia the level of the anesthesia must be watched carefully. During high spinal anesthesia the intercostal muscles are paralyzed; the patient may feel short of breath, and it is necessary to give oxygen. The level of spinal anesthesia may be high enough to paralyze all the intercostal muscles and the diaphragm. When this occurs, it is necessary to perform intubation and give artificial respiration. In England this is the procedure used for some operations. Needless to say, it is somewhat distressing to the anesthetist.

An ever present danger is that of a sensitivity reaction to a local anesthetic agent. The reaction may be severe, with convulsions, cessation of respiration, and shock. Therapy must be instituted promptly and should include barbiturates given intravenously, artificial respiration, and ephedrine. Means for carrying out such therapy should be avail-

able whenever and wherever local anesthetic agents are used.

The treatment of respiratory emergencies is important not only because of their effects per se, but also because of their effects on the circulation. The maintenance of one function depends on maintenance of the other; however, the patient is better able to tolerate lack of respiration than lack of circulation.

CARDIOVASCULAR EMERGENCIES

We have two very important guides to the condition of the circulation: the pulse and the blood pressure. By measuring these and correlating the measurements, we have a good idea of the condition of the vascular system of the patient. The record of pulse and blood pressure is a drawing of the circulatory status.

A record showing a decreasing blood pressure with decreased pulse pressure and tachycardia means one thing: shock. The patient begins to perspire freely and looks pale; the pulse becomes less perceptible to palpation; respiration may show evidence of air hunger. Why is the patient in a state of shock? This condition is not always due to loss of blood; it may be due to several other factors, such as trauma from the surgical procedure or too deep a level of anesthesia.

We have all seen the patient who has not lost appreciable amounts of blood but whose blood pressure steadily decreases; also, according to accepted criteria, the level of anesthesia is not deep, and the operation is performed with a minimum of trauma. It is amazing how quickly such a patient will respond to a transfusion.

In preparation for all major procedures, especially for thoracic surgery and neurosurgery, a needle should be inserted into a vein. Blood spurting from a pulmonary artery or a major vessel is a startling sight. Here it is not a question of minutes but of seconds. The blood pressure may decrease from 120-80 mm. Hg to being imperceptible while it is being measured. For this type of operation a 15 to 17 gage needle should be in a vein, blood should be available in the operating room, and the anesthetist should be prepared to take over respiration at any moment. If positive pressure is being used, blood pressure may decrease and tachycardia occur as a result of the resistance to the pulmonary circulation and poor filling of the heart.

During operations on the brain there is frequently a gradual decrease in blood pressure. The neurosurgeon usually prefers to have the blood pressure low since decreased bleeding facilitates the operation and hemostasis. However, the blood pressure should not be allowed to decrease below 80-90 mm. Hg systolic. Once the intracranial part of the procedure is finished, the blood pressure should be increased as rapidly as possible.

In other cases of shock steps should be taken to return the blood pressure to normal levels as rapidly as possible, for a patient does not tolerate shock for any length of time. The first organs to suffer are the kidneys with danger of permanent damage; even if this does not happen, a stormy postoperative course will ensue.

When low blood pressure is due to too deep a level of anesthesia, the anesthesia should be lightened immediately. No surgeon should demand a depth of anesthesia that produces shock.

Hypotension with a decreased pulse pressure and bradycardia is associated with the decrease in

blood pressure during spinal anesthesia. Prophylaxis for the condition is the administration of ephedrine prespinally before a decrease in blood pressure occurs.

If this situation does occur, the best treatment is the use of ephedrine, 25-50 mg., or neosynephrin, 5-10 mg., to increase the pressure to normal levels. If this is not effective, the administration of plasma or even blood may be necessary. As a matter of fact, if the use of these drugs does not increase the pressure to normal levels in fifteen to twenty minutes, plasma should be given.

Hypotension associated with traction on viscera is usually sudden and is associated with bradycardia. It is usually relieved with the release of the traction; if it persists, it is wise to resort to the use of vasopressor drugs.

One of the commonest causes of hypertension is the accumulation of carbon dioxide. This type of hypertension is usually associated with no change in the pulse except an increased volume.

The accumulation of carbon dioxide is not always associated with deficient soda lime but may occur when the respiration is depressed by deep anesthesia or any other cause. If the bag is flushed out with oxygen to remove excess carbon dioxide and the anesthesia is lightened, if deep anesthesia is responsible, the blood pressure will return to normal limits. Hypertension with increased pulse pressure and tachycardia is most frequently associated with anoxia and asphyxia and should be corrected immediately.

Arrhythmias are a source of great concern to the anesthetist. One of the commonest is premature contraction of the heart, or extrasystoles, and is most prone to occur in patients having previous cardiac disease. The type of arrhythmia may range from extrasystoles to ventricular fibrillation.

The causes of the arrhythmias are respiratory depression from any cause, use of epinephrine in conjunction with anesthetic drugs, too deep anesthesia, and vagal stimulation from surgical procedures around the hilus of the lung, especially during cardiac surgery.

The best treatment is to lighten the anesthesia and, if necessary, change the agent. The greatest incidence of arrhythmias occurs during cardiac surgery. There may be sudden cardiac standstill that clears up as soon as traction on the heart is released and the heart is massaged. One of the best means of combating the condition is for the surgeon adequately to procainize the heart. The same effect may be obtained by giving 0.1 per cent procaine intravenously in 1,000 cc. of normal saline. The rate of flow to prevent arrhythmias varies with the individual requirement of the patient. The amount given should be kept below that which will produce facial twitching. Since procaine is a cortical convulsant, it must be used with great care.

I am sure that we have all, unfortunately, experienced that horrifying moment when we have realized that the patient's heart has stopped. If the chest is open, the surgeon is usually cognizant of the fact and can institute gentle cardiac massage. The anesthetist should start artificial respiration immediately. If the chest is not open, the surgeon can carry out massage through the diaphragm, either open or closed, for at least twenty or thirty minutes. By careful vigilance and the maintenance of an adequate airway and veinway, the anesthetist can meet any emergency that occurs and usually win.

CURARE

Ruth C. Martin, M.D.*
Durham, N. C.

HISTORY

Curare, or Indian arrow poison, has been used for many generations by various savage tribes, particularly the South American Indians. It has been known to medical science for about 100 years. It was first described by Hakluyt in his *Voyages and Discoveries,* in which he related how Sir Walter Raleigh in 1595 met Indians of the Upper Amazon and brought back curare as well as tobacco to England.

South American natives still use gum curare upon arrow tips to paralyze game in hunting. The edibility of the animal is not impaired, since curare is innocuous when taken into the alimentary tract. Either it is destroyed in the intestinal tract, or absorption is so slow that effective concentrations are not reached in the blood stream.

In 1815 Watterton and Brodie demonstrated asphyxia to be the cause of death in curarized animals.

In 1840 Claude Bernard demonstrated that the site of action of curare is at the myoneural junction. Bernard showed: (1) that the drug must enter the body by some route other than the alimentary tract in order to be effective, (2) that the sensory mechanism is not affected, (3) that the action of the drug produces no irreversible change in the muscle or the nerve, and (4) that the cardiovascular system is not directly affected by the drug.

In 1938 Richard C. Gill, an American who had lived for years in the upper Amazonian jungles of Ecuador, brought to the United States the first adequate supply of the drug with properly labeled specimens of the various plants that are used by the Indians in the manufacture of crude curare. Professor A. R. McIntyre of the University of Nebraska then subjected this supply of curare to the first pharmacologic study by modern methods. The commercial product first placed on the market bears the trade name of Intocostrin. Intocostrin, a pale amber liquid, is marketed in 10 cc. vials, each cubic centimeter of which contains 20 mg. of active curare substance. When Intocostrin is used, the terms milligrams and units are used interchangeably. More recently a purified product known as *d*-tubocurarine has become available. Most pharmaceutical houses marketing *d*-tubocurarine prepare solutions in such a way that 1 cc. of the liquid contains an amount of crystalline alkaloid equivalent to 20 units of Intocostrin; only 2.7 mg. of the alkaloid salt of curare is present in each cubic centimeter.

The assay method depends upon the fact that the voluntary musculature is selectively affected; the short muscles of the eye and neck, i.e., muscles of high chronaxia, are affected first. The curare solution is injected slowly into an ear vein of a rabbit and the dose adjusted so that the neck muscles reach a degree of

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*Director, Division of Anesthesiology, Duke University.

flaccidity that prevents the animal from raising its head. The amount per kilogram necessary to produce this effect is estimated and the dosage figured according to the body weight of the animal.

The first large scale test of curare on human subjects was made by Professor A. E. Bennett of the University of Nebraska; he used it to soften the traumatic effects of convulsive shock therapy in psychiatric patients.

In 1942 Dr. Harold Griffith at the Homeopathic Hospital of Montreal began using curare in patients under cyclopropane anesthesia.

PHARMACOLOGY

Curare, acting peripherally, paralyzes skeletal musculature progressively and quantitatively. The muscles of cranial innervation are affected first, then the muscles of the trunk and extremities, and last the diaphragm. The differential paralysis of all somatic muscles except those necessary for respiration may be produced. The basic action of curare is its ability to minimize or prevent the response of receptor cells to acetylcholine. There is no decrease in the amount of acetylcholine produced at cholinergic nerve terminals. The effect of the drug is directly proportional to its concentration at the site of action. The action is reversible and can be reversed by increasing the concentration or the length of action of acetylcholine. One can increase the concentration or prolong the action of acetylcholine by: (1) strengthening the nerve impulse, (2) adding acetylcholine artificially, and (3) inhibiting the action of cholinesterase.

Injection of prostigmine, which is known to inhibit cholinesterase, is the most convenient method of reversing the curare effect. The dose given is 1-2 cc. of 1:2,000 or 1:4,000 solution of prostigmine methylsulfate.

If its action were limited to skeletal muscle, curare would be the perfect drug for use in anesthesia. However, in increasing dosage it appears to affect the autonomic nervous system and the central nervous system. As you know, acetylcholine is the chemical transmitter of impulses at the sympathetic and parasympathetic ganglions and is released at the terminals of all cholinergic nerves.

Whitacre and Fisher gave huge doses of curare to unanesthetized patients and produced complete respiratory arrest and loss of consciousness. Artificial respiration was instituted and maintained during the operative procedures. Their dosages were approximately four times as large as those which we employ. They found administration of the drug in this manner to be unsatisfactory and abandoned the method.

Electrocardiographic studies of normal and of abnormal hearts fail to show any influence of the administration of therapeutic amounts of curare. Large amounts given intravenously in a short time or moderately large doses given repeatedly for a long time may cause peripheral circulatory depression and a decrease in blood pressure due to: (1) a direct relaxing effect on the smooth muscles of the arterioles, or due to (2) loss of vasomotor tone caused by interference with the transmission between preganglionic fibers in the sympathetic ganglions, or merely as a result of (3) widespread muscle relaxation with consequent impaired venous return and lowered cardiac output.

The circulatory depression is usually of brief duration, and recovery occurs without specific therapy. In

patients with labile vascular systems it may be profound and refractory to treatment.

The amount of curare required for relaxation of the abdominal muscles causes cessation of peristalsis of the small intestines for two to three minutes and loss of tone for about twenty minutes. This effect is due: (1) to the direct curare effect on isolated gut, and (2) to the fact that curare blocks the action of the vagus nerve to some extent.

Morphine and cyclopropane obliterate the curare effect on the small intestines.

DESTRUCTION

There is minimal destruction of curare in the liver; most of it is excreted unchanged by the kidney. Liver and kidney disease have not been shown to be contraindications to its use.

TECHNIC OF ADMINISTRATION

When curare is to be used, atropine or scopolamine must be given prior to its administration, for it does not block the muscarinic action of acetylcholine, and the secretion of a profuse amount of thick tenacious mucus may be troublesome or dangerous. The dosage of morphine or barbiturates given preoperatively will depend on the agent chosen to be used with the curare.

Since curare has no analgesic action, it must be used in conjunction with some general anesthetic agent. As a rule, we use ethylene or cyclopropane to produce lower first or early second plane anesthesia. Injected intravenously, curare acts within forty to sixty seconds, and its full effect is produced in three minutes. The duration of action is about twenty minutes. The muscles of the abdominal wall have the same group innervation as intercostal muscles. Therefore, if, by the time the peritoneum is reached, the intercostal muscles are not lagging or retracting slightly on inspiration, another cubic centimeter is given. Additional drug is injected when needed, but in the average case none need be added until the peritoneum is to be closed.

While pharmacologic evidence suggests that the excretion of curare is very rapid, and that a physiologic dose may be safely repeated within twenty minutes, animal experiments have shown that the drug may have some cumulative action. Our own experience indicates that adequate relaxation may be obtained by a second and subsequent doses smaller than the initial injection.

In debilitated patients or in those with very labile blood pressure, our initial dose is 1 cc. with subsequent doses of the same size given at intervals until satisfactory relaxation is produced. We do this to avoid the circulatory depression that I have mentioned.

If intercostal activity is markedly impaired, the diaphragm will descend in a jerky fashion that is troublesome in gallbladder surgery. Respiration, if shallow, must be supplemented by gentle pressure on the breathing bag during the inspiratory phase, for hypoxia will cause muscular rigidity even though the myoneural junctions have been paralyzed. Also, lack of oxygen or excess of carbon dioxide will cause jerky respiratory efforts in patients who have received a dose of curare that would otherwise be ample to cause apnea.

If curare is given to a patient too lightly anesthetized with a general anesthetic, muscular spasms, including bronchiolar spasm, diaphragmatic contractions, and slight twitchings of the facial muscles,

may result. There may be an increase or decrease in blood pressure. These signs are indications not for more curare but for more anesthetic, for adequate general anesthesia prevents reflex stimulation and the nullification of the curare effect.

Ethyl ether, pentothal sodium, and avertin have been shown to possess curariform properties, in the sense that they inhibit the contractile response of a muscle in a dog to an injection of acetylcholine and to an electric stimulation of the controlling nerve. Of these three anesthetics, ether is the worst offender; high blood concentrations of pentothal sodium and avertin are required to demonstrate this effect. When used with avertin or pentothal sodium, the curare dosage required for the gases must be cut in half; when used with ether, approximately one third of the usual dose is required.

Pentothal Sodium and Curare

If curare is to be used with pentothal sodium, certain things must be kept in mind:

1. Pentothal sodium has a curariform action of its own; hence, curare must be given cautiously and in small doses.
2. Curare depresses respiration peripherally owing to its effect on the intercostal muscles, while pentothal sodium causes a central depression of respiration.
3. Intocostrin precipitates pentothal sodium. *d*-Tubocurarine does not cause precipitation of pentothal sodium, and many workers are now advocating the use of *d*-tubocurarine-pentothal sodium mixtures. It is claimed by those using such solutions that the curare potentiates the pentothal sodium effect and markedly reduces the quantity of barbiturate required.

Ether and Curare

In 20 mg. doses, curare improves relaxation in first plane, ether anesthesia, while large doses of 100 mg. or more may precipitate severe circulatory depression. In the presence of deep ether anesthesia, even small doses of curare may cause marked circulatory reactions. In one clinic the intravenous injection of 20 mg. of curare in one patient in the third plane of anesthesia caused complete peripheral circulatory failure. The circulation was restored by promptly decreasing the depth of inhalation anesthesia. If sufficient ether has been given to produce third plane anesthesia and relaxation is still unsatisfactory, it is probably unwise to use curare.

Uses of Curare

Curare is now used for many purposes other than to obtain relaxation for abdominal surgery. We used it in a few instances to produce relaxation for the reduction of fractures. The only disadvantage to this practice is that the procedure is a short one, and the patient is allowed to wake up before the full curare effect has worn off. Inability to talk or to focus his eyes for a time is disturbing to the patient.

We believe that laryngoscopy and short operative procedures involving the larynx can be best performed under a combination of topical anesthesia, *d*-tubocurarine, and pentothal sodium.

I have mentioned its use in psychiatry to prevent fractures of the long bones and compression frac-

tures of the vertebrae during metrazol or electric shock treatment.

In cases of paralysis agitans, athetoid disorders, multiple sclerosis, Huntington's chorea, spasmodic torticollis, etc., curare noticeably diminishes the hypertonia, tremor, and involuntary motility.

In spastic children with fixed deformity, curare causes a transient relaxing effect which reduces the inco-ordination, athetosis, and dysarthria and permits carrying out physical therapy under more favorable conditions. In patients in the acute stage of poliomyelitis, curare has been used to decrease the nuchal rigidity, opisthotonos, and spasms of other muscles.

The drug may be used in minute doses in a diagnostic procedure for myasthenia gravis and often gives a strongly positive test even when the opposite prostigmine test is indefinite. When it is so used, its effect must be promptly terminated by the intravenous injection of prostigmine, or the patient's life will be endangered.

Some workers used curare in the treatment of hiccoughs and found that 40 mg. relieved patients for as long as eight hours.

One gynecologist used curare in the treatment of 43 cases of severe dysmenorrhea and found that such disabilities as cramps, nausea, backache, and dizziness were relieved two to fifteen minutes after intravenous injection of the drug.

From time to time, since 1894, curare has been used in the treatment of tetanus. We treated three patients with it, administering it by both the intravenous and the intramuscular route. We found that the dosage required was large and that the muscular spasms were relieved for only two to three hours with a single injection. It was necessary to have an anesthetic machine, intratracheal equipment, and prostigmine at hand in case of undue respiratory depression. This tied up too much of our equipment and proved impracticable. Patients could not be kept atropinized for periods of days, and the thick, tenacious secretions that appeared following curare injection proved to be both troublesome and dangerous.

Just as we were beginning to believe that we understood curare and its administration, Landmesser and Dripps of the Department of Anesthesia of the University of Pennsylvania further complicated the picture by describing the histamine-like action of the drug. He found that Intocostrin produced typical histamine-like wheals when injected intracutaneously or intra-arterially in man. He postulated that the bronchiolar spasms that have been reported may be due to this histamine-like action as well as the decrease in blood pressure following injection of large doses of curare. The histamine-like actions of curare are not antagonized by prostigmine since the latter drug overcomes only the paralyzing effect upon the myoneural junction. Pyribenzamine, a new antihistamine agent, is the drug of choice at the present time for combating such reactions.

ADVANTAGES

An evaluation of curare is difficult at this time because of the newness of the drug. We have found that:

1. It is well tolerated by patients with severe cardiac disease. Blood pressure fluctuation rarely occurs in such patients, and we have not encountered any disturbances in cardiac rhythm.

2. If the inhalation anesthesia is properly managed, curare produces relaxation comparable to that produced by spinal anesthesia. We have had poor relaxation in some cases, but in retrospect we believe that inadequate general anesthesia was the reason for this in the great majority of such instances.
3. The amount of general anesthesia required is markedly reduced, and the patients are awake before or shortly after they leave the operating room.
4. Also, less time is required to prepare a patient for operation with gas-curare anesthesia than with continuous spinal anesthesia.

Disadvantages

1. All signs of depth of anesthesia with inhalation agents are lost. The signs which we usually rely on are eyeball movements and respiratory activity. The eye muscles are paralyzed, as are the intercostal muscles to a lesser degree. The anesthetist must therefore be thoroughly familiar with the inhalation agent which she is using and must develop a seventh sense if she is to avoid too deep or too light anesthesia and their attendant dangers.
2. The margin between intercostal and diaphragmatic paralysis is often narrow. If the diaphragm is paralyzed, it is a simple matter to control respirations by gentle pressure on the breathing bag until diaphragmatic function returns, but an inexperienced anesthetist could damage the patient's lungs with this maneuver.
3. Because of the marked relaxation of the throat muscles, an intratracheal tube must be quickly inserted in some cases. Anesthetists unskilled in intubation should never give curare. The vocal cords are paralyzed to some extent, and the danger of aspiration of stomach content is increased. An intratracheal tube with an inflatable cuff should be used in cases of intestinal obstruction or in other cases where there is danger of regurgitation of stomach or intestinal contents.
4. Complications such as bronchiolar spasm must be recognized at once and properly treated. If the blood pressure increases or decreases, the anesthetist must know the reason for the change and must remedy the situation at once.

Summary

The use of curare as an adjunct to anesthesia places additional demands on the anesthetist, and in the final analysis the success or failure of this method, probably more than of other methods now in use, depends more on the skill and knowledge of the administrator than on the drug itself.

CEREBRAL MANIFESTATIONS OF ANOXIA

A Review of the Literature
PART I

Florence A. McQuillen, R. N.*
Chicago

The dangers of anoxia have been apparent since long before the discovery of surgical anesthesia. The immediate consequences of oxygen deprivation are sufficiently violent and spectacular to elicit prompt recognition and corrective measures. Asphyxial phenomena are associated with situations other than anesthesia in so many ways that not only the medical profession but the general reading public is constantly made aware of its dangers. Entire societies have been formed to teach the preventive and corrective measures necessary in accidental asphyxiation.

Smoke, poisons, gases other than anesthetics, drowning, varying atmospheric pressures, suffocation, diseases, and shock are among the multitude of causes of anoxia. The results of studies made in all of these phases of asphyxial incidents may be of value to the anesthetist in the specific study of anoxia associated with anesthesia. Particularly, the studies of anoxia in relation to aviation are of interest because from them the modifications of asphyxial signs that occur as the result of anesthesia may be determined.

EXPERIMENTAL STUDIES WITH ANIMALS

Experimental studies of anoxia and its effect on the cerebral cortex produced a wealth of information, some of it contradictory. Yant et al[161] studied the neuropathy associated with carbon monoxide, carbon dioxide, and oxygen-deficient atmospheres. Dogs and rats were studied in atmospheres containing from 2.26 per cent to 8 per cent of oxygen for from eleven to twenty-five minutes (dogs) and twenty-four to seventy-two minutes (rats). There was marked difference in the susceptibility of the nerve cells to deprivation of oxygen; the cells of the cortex of the brain were most sensitive. Dogs asphyxiated by atmospheres deficient in oxygen died in less than thirty minutes.

Weinberger et al[152] found that following temporary arrest of circulation of the central nervous system, pathologic lesions were evident in animals after three minutes and ten seconds. Necrosis and softening of the cortex were followed by more severe damage as the time increased, liquefaction resulting after seven minutes.

Hartman,[69] in considering the etiologic factors in cerebral anoxia, concluded that all lesions of the cerebral cortex, whether the cause is shock, sedation, or fever, are rather uniform when all factors are considered.

Gomez and Pike[57] ligated the carotid and subclavian arteries of animals and found that "with the return of the circulation, dilatation of the pericellular lymph space and slight swelling of the cell body occurs, disappearing as recovery prog-

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*Executive Director, A.A.N.A.; Co-editor *Anesthesia Abstracts.*

resses. Chromatolysis . . . induced by anemia is not necessarily fatal. . . . Neurones from different regions as well as neurones of the same regions differ in degree of resistance to anemia. . . . Failure to resuscitate animals after anemia of the central nervous system is probably due to the destruction of many of the cells of the vital centers (vaso-motor and respiratory) which do not have histological peculiarities by which they may be defined. Death, however, of a few cells of any center does not necessarily mean the total loss of function of that center since the remaining cells may be sufficient to discharge the functions of the center."

Gildea and Cobb,[53] also studying the effects of anemia on the cerebral cortex in experiments on cats, found indications that periods of anemia of not more than ten minutes result in permanent injury to the cortex and not uncommonly in changes that end in death from convulsions or failure of the respiratory center.

Kessler et al,[86] who studied the effect of anoxic anoxia on the central nervous system in rats, concluded that the effects were pharmacologic rather than physiologic. Thorner and Lewy[143] produced repeated sublethal anoxia in guinea pigs and cats. They concluded that irreversible, summate lowering of the cerebral reserve followed repeated episodes of anoxia. Using pure nitrogen in their experiments they concluded that guinea pigs, immersed in an atmosphere deficient in oxygen, "behave in a somewhat stereotyped manner. There is usually an almost immediate increase in the respiratory rate. In from ten and fifteen seconds the animal becomes very active, in another 20 seconds the animal shows some arching of the neck and then slumps to the floor of the container. The retinal light reflex, ear, tongue and mucous membranes appear cyanotic. Spasmodic movements may be seen, varying from isolated chronic twitching to generalized convulsions. If the animal is immersed for more than one minute, it is usually apneic when removed and must be given artificial respiration. . . . Exposures to sublethal periods of pure anoxia lead to vascular and degenerative changes in the brains of guinea pigs and cats. Some of these changes are irreversible and become summated in animals repeatedly subjected to anoxia."

Weinberger et al,[152] studying the effects of temporary arrest of the circulation of cats, found that, following three minutes and ten seconds or less of circulatory arrest, there were no obvious neurologic disturbances. After the circulation was arrested for three minutes and twenty-five seconds, alterations in behavior and psychic functions resulted. After six minutes' arrest, evidence of disturbances of vision and sensation of permanent nature resulted. Seven minutes and thirty-six seconds of circulatory arrest produced permanent and practically complete dementia: blindness, sensory, and auditory defects, motor and postural defects, and reflex abnormalities. When the arrest of circulation was prolonged to eight minutes and forty-five seconds, life could not be restored for more than a few hours.

Experimental Studies in Human Subjects

Haldane[64] in 1919 discussed the symptoms, causes, and prevention of anoxemia. He concluded that "whenever a comparatively slight anoxaemia . . . is continued for several hours, the common result is

nausea, headache and general depression. . . . When the anoxaemia is more severe, the evidence of progressive damage becomes more and more marked, so that even when the cause of anoxaemia is completely removed grave symptoms may remain." This is only one of many discussions of the anoxic phenomena that have resulted from studies of oxygen deprivation in aviation.

McFarland[102] (1932) studied air squadrons at partial pressures equivalent to altitudes of 17,000 to 28,000 feet. He found that simple sensory and motor responses were not seriously impaired until collapse. Choice reactions were impaired when oxygen was reduced to 11.43 per cent. Neuromuscular control was lost before capacity. Tremors and twitchings occurred. Memory was impaired at an average of 9.05 per cent oxygen and was in proportion to the extent of deprivation. Attention was greatly affected. Higher mental processes were affected; ideas became irrational or fixed and capacity for judgment and self criticism was lost. Slight oxygen deprivation produced stimulation of moods, followed by sleepiness, lethargy, and indifference. At 9.05 per cent, loss of ethical and moral habits occurred. Hysterical laughter, anger, or sleep was common. These reactions were compared to phases of alcoholism. These studies "tend to show the importance of one's basic physiological make-up in the formation of one's personality."

Actual cases of oxygen deprivation during flight have been reported. Among these are the report by Ward and Olson[147] of a 21 year old aviator who was found unconscious and apneic after being deprived of oxygen at an altitude of 25,000 feet for thirty-nine minutes and at an altitude of 12,000 feet for an additional sixteen minutes. For eighteen hours after resuscitation he remained in coma. He then became alert, elated, and talkative. Logic, judgment, and memory were poor. On the second day he vomited. His mental state remained the same as the previous day. After seven weeks the mental state was entirely normal. Titrud and Haymaker[144] reported three cases of oxygen deprivation during flight. A 21 year old aviator was found unconscious after a flight at 20,000 feet. Oxygen and artificial respiration were administered. Convulsions and delirium developed. Death occurred forty-eight hours later. Study of the brain showed widespread necrosis of ganglion cells. Damage was of such extent as to equal decerebration. A second incident involved a 22 year old aviator who was deprived of oxygen for a period of ten minutes during a flight at 24,000 feet. Oxygen and artificial respiration were administered. Convulsions developed on the ninth day. Death occurred on the twenty-first day after the episode of anoxia. Examination of the brain showed extensive damage. A third young man who was deprived of oxygen during combat was discovered one and one-half hours later, cyanotic and delirious. He recovered, but when he was transferred from the hospital three weeks later, he was severely retarded both physically and mentally.

ANOXIA AND ANESTHESIA

Cyanosis, asphyxia, and anoxia have been subjects of interest since before the discovery of anesthetics. Following the idea through examples of thought as they appear in the literature, wavering near and often far from the idea, the thread of the effects of anoxia during

anesthesia can be traced from the first publications on the subject of anesthesia.

W. T. G. Morton[109] in his "Remarks on the proper mode of administering sulphuric ether by inhalation," published in 1847, said: "The vapor of sulphuric ether, as is well known, will not support life in its pure and unmixed state, being destitute of oxygen; and fears were entertained, when it was first applied to its present use, that, unless extreme care was taken to supply the patient with a large amount of atmospheric air, not enough oxygen would enter the lungs to decarbonize the blood and change it from venous to arterial; venous blood would then be sent to the brain, and the patient die from asphyxia, in the same manner as when deprived of oxygen by immersion in water, or from any other cause." The subject was even part of the controversy. In his *Memoir on Sulphuric Ether,* also published in 1847, Morton[108] wrote: "On that day [January 2, 1847], he [Jackson] called at the hospital with some oxygen gas as an antidote for asphyxia, which he heard was produced by the ether."

Snow[135] in his book published in 1847 referred to stertorous breathing and commented that "I have, however, never known it to leave any cerebral symptoms afterward." He also presented a case of a man, 49 years of age, who developed spectral illusions for a week or two after operation. He had been given ether twice within twenty minutes. Snow had "not heard of anything of the kind after ether in any other case."

In 1887 Buxton,[15] outlining the physiologic action of nitrous oxide gas, commented: "Whatever may be the saving of gas brought about by employing supplemental bags wherein the nitrous oxide is collected and re-inspired again and again, the patient suffers by their use from the double evil of breathing diluted and impure nitrous oxide, and further, is not favourably placed for exhaling the refuse of the lungs. I should incline to attribute to this method the cases one occasionally meets with of severe headache, vertigo, dizziness and other untoward symptoms consecutive upon nitrous oxide inhalation." He experimented on dogs whose brains during oxygen deprivation were observed through trephine openings.

Jackson[81] (1894) conducted experiments on dogs to determine the cause of the intensification of lateral deviation of the eyes in a case of hemiplegia during chloroform anesthesia. He concluded that the phenomenon was the result of insufficient circulatory compensation of the brain.

Buxton[16] (1897), reporting the death of a nurse during nitrous oxide and ether anesthesia for the extraction of teeth, warned of the dangers of oxygen deprivation and asphyxia. He made an additional observation that is still pertinent today: The accidents that occur during anesthesia often appear "in press but not in professional journals."

Hewitt[74] (1899), in discussing deaths during nitrous oxide anesthesia, said that almost always deaths from asphyxia were the result of obstruction. He observed that "when nitrous oxide is administered free from oxygen, asphyxial phenomena arise; obstructive stertor, convulsive muscular movement and cyanosis."

King[87] (1904), following the recovery of two patients after apparent death under chloroform, concluded that deaths under chloroform

were not, as was usually thought, the result of cardiac failure but were respiratory in nature.

Miller[104] (1912) investigated postoperative mortality from anesthetics and said that "Death during or following an operation is due to the anesthetic if the death would not have occurred under an ideal anesthetic."

Warner[148] (1915) pointed out that "perfectly normal color can be maintained while the patient is presenting all symptoms of asphyxia including convulsions."

Barcroft[7] (1920) said: "No degree of anoxaemia which produces a less effect than that of complete unconsciousness leaves anything more than the most transient effects; if the anoxaemia be pushed to the point at which the subject is within a measurable distance of death, the results may take days or weeks to get over, but only in the case of elderly or unsound persons is the machine wrecked beyond repair. . . . Just as acute anoxaemia simulates drunkenness chronic anoxaemia simulates fatigue. Another symptom frequently associated with mental fatigue is irritability."

Grant[59] (1923) after experiments concluded that anoxemia plays no part in the causation of tetany during hyperpnea.

Henderson[72] and many others have persistently preached the doctrine of asphyxial phenomena and their prevention.

Others have explored the postanesthetic phenomena, often approaching but also often overlooking the role of anoxia (Kaye,[84,85] Miller,[105] Nelson[111,112]).

Macklin[97] (1931) concluded that "neither practically nor theoretically can a carefully controlled anoxaemia be regarded as a contra-indication to [the use of nitrous oxide]."

Moore [107] (1934) stated that the presence of cyanosis "is no indication of actual danger, nor is its absence a sign of entire safety."

Raginsky and Bourne[121] (1934) expressed the opinion that the 80:20 mixture of nitrous oxide and oxygen is insufficient for some human beings.

Flagg[41] has been among a group of persistent writers on the subject of prevention of asphyxia.

Harris[68] (1937), as well as others, made a vigorous statement in behalf of adequate oxygenation. "Anoxia, employed in anaesthesia can only be looked upon as an additional burden thrown upon the tissues of the body already subjected to the unphysiological strain of the anaesthetic agent. One must therefore conclude that the use of anoxia as an adjuvant in anaesthesia is unsound, while the Secondary Saturation of McKesson is to be heartily condemned."

Lawrence[90] in 1937 suggested that percentages of oxygen sufficient to meet metabolic requirements were necessary to safe nitrous oxide anesthesia.

Bennett and Seevers[17] (1937), studying anoxia in human subjects, concluded that "Experimental studies . . . substantiate the common clinical observation that anoxia is a necessary accompaniment of deep anesthesia with nitrous oxide in the subject who has not received previous depressant drug medication."

The specific designation of the role of anoxia in cerebral damage following anesthesia was brought to the attention of anesthetists in 1936 in a monograph by Courville.[20] In the introduction he stated: "On the basis of the evidence at hand, it seems evident, therefore, that varying degrees of anoxemia do exist and are necessary in the production of anesthesia with nitrous oxide and

that cellular asphyxia strongly reinforces any direct narcotic action of the gas. As the higher concentrations of nitrous oxide are reached, there always exists the danger of irrevocable damage to the brain. Should even a transient respiratory and circulatory failure occur under anesthesia, asphyxia of the cortical nerve cells occurs after the utilization of the small amount of available oxygen." Continued evidence seems to indicate that the foregoing statement could be modified to include other anesthetics.

Gellhorn[50] (1937) reported experiments on the effects of anoxia. "Systematic investigations were carried out in which the influence of oxygen deficiency, excess of carbon dioxide and voluntary heavy breathing (hyperpnea) were studied in relation to various sensory functions, motor coordination, psychic processes, and subcortical reflexes. As to the sensory functions which were mediated by the cortex, it was found that auditory acuity and visual intensity discrimination were greatly decreased under all three conditions. Similar results were obtained with respect to visual afterimages. Various psychic processes, such as formation of associations, the cancellation of a number (Bourdon's test), the addition of two digits (Kraepelin's Test), were investigated with respect to the effects of the three factors mentioned above, and here it was found again that under all three conditions the psychic processes were influenced in a similar fashion. There were only quantitative differences, the changes produced by oxygen deficiency being most severe. . . . All the phenomena were, in most cases, more or less immediately reversible upon readmission of air. . . . In contradistinction to these results it was found that the physiologic processes involving the lower part of the brain (brain stem) and not the cortex, showed a different reaction. . . . These investigations seem to indicate that the psychic processes are cortical phenomena which depend on and are modified by the same physiologic factors which influence ordinary physiologic processes."

In discussing cerebral anoxemia Soley and Jump[136] (1939) stated: "Judging from the usual pre-operative case history . . . it is not generally considered important to question the patient as to incidents which could have resulted in anatomical changes due to asphyxia . . . Even though one were to attempt to elicit a history of asphyxia from a patient, it would be difficult to be sure that the history was reliable."

Behrend and Riggs[10] (1940) discussed predisposing factors, prevention, and treatment of cerebral complications following operation. "In the cases studied by us, anoxia was usually secondary to acute general circulatory collapse precipitated by administration of an anesthetic plus the trauma of operation in patients whose margin of circulatory reserve had been reduced."

Wynne[160] (1940) studied the relation of cyanosis and anoxemia and prepared a chart showing the relation of blood components to cyanosis.

Some authorities maintain that undesirable effects of nitrous oxide anesthesia are a manifestation of a toxic action of nitrous oxide, while others contend that such effects are the result of anoxia. Murphy[110] (1940) affirmed the latter opinion: "It has been accepted by clinical anesthetists . . . that nitrous oxide is neither toxic, in the ordinary sense, nor is it irritating to the tissue. . . . The abandonment of the secondary saturation techniques, the

promiscuous use of nitrous oxide by unskilled attendants . . . and the 'pushing' of nitrous oxide in surgical cases, will soon prove that asphyxia not anesthesia with nitrous oxide is responsible for the untoward effects which recently have been receiving attention."

The work of Waters[150] (1940) (1944) exemplified the increasing interest and concern of anesthetists in the subject of anoxia in relation to anesthesia. McCarthy[99,100] (1941) (1942) also emphasized the interest in the dangers and prevention of anoxia. "There is a real danger that serious complications may be produced by anoxia incident to nitrous oxide anesthesia. This is always an indication of technical error that may be avoided by proper care in administration and by close observation of the patient for signs of oxygen want."

Batten[8] (1942) in discussing the hazards of hypoxia suggested that: (1) the avoidance of the promiscuous use of respiratory depressant drugs, (2) administration of not less than 20 per cent oxygen with nitrous oxide, (3) maintenance of normal levels of respiration, pulse, and blood pressure, (4) postanesthetic care, (5) oxygen inhalations when signs of hypoxia appear, and (6) curtailment of the use of spinal anesthetics would reduce the dangers.

Horvath et al[77] (1943), in studying schizophrenic patients subjected to reduced oxygen concentrations to the point of unconsciousness, concluded that "anoxia severe enough to produce brief periods of unconsciousness has no lasting harmful effects on the central nervous system."

POSTOPERATIVE PSYCHOSIS

The search for the cause of the cerebral sequelae of operations has included study of factors other than anesthesia. Postoperative psychosis has been recognized as a complication of operations since before the discovery of surgical anesthesia. Ambrose Paré mentioned the occurrence of mental symptoms after operations.

Some of the causes of psychotic episodes have been variously stated as familial tendencies, drug allergy, fever, fear, worry, epilepsy, sepsis, senility, and hysteria.[3,123] Psychoses are known to have followed the use of many drugs without the addition of surgical intervention. Among the many drugs known to have produced such episodes are a group often used in treating conditions before or during anesthesia. Gage-Day[46] (1909) listed among other drugs which caused acute toxic insanities, chloral, morphine, alcohol, chloroform, ether, and paraldehyde. Danziger[26] (1945) listed the compounds that have been known to cause symptoms of mental disorders in man. He stated: "It is suggested that anoxia is a sufficient and perhaps a necessary condition for the development of abnormal behavior."

Da Costa[25] (1910) included among other causes of postoperative psychoses the possibilities that the "anesthetic may poison" the patient and that disturbances of cerebral circulation may occur.

Woltman[157] (1939) in commenting on postoperative neurologic complications said: "Immediately, or several days after operation, lead-pipe rigidity may develop in the patient. It is a serious omen that some patients slip into this state and out of it again and recover. . . . A somewhat similar condition, but resembling decerebrate rigidity, has been observed after spinal anesthesia in which the usual dose has been administered to a patient who has profound anemia. . . . [The com-

monest type of psychosis] does not begin immediately after operation but begins after an interval of about five days and lasts for about two weeks. . . . It seems significant that when the psychosis is a 'postoperative psychosis' in the restricted sense of the term, anesthesia is almost always by inhalation and usually includes ether. . . . Most postoperative mental disorders . . . belong to the restricted group of postoperative psychoses. Next in frequency is the group which may safely be called toxic-infective-exhaustive psychoses, in which the psychoses immediately preceding and following operations usually are included. These in turn are followed by the deficiencies, the manic-depressive group and finally by the senile, schizoid, epileptoid, mentally unstable and other groups."

Doyle[32] (1928), in reporting twenty-eight cases of postoperative psychosis, suggested that the term "post-anesthetic psychosis" be used for disturbed mental conditions which immediately follow operation and that the term "postoperative psychosis" be used for mental disturbances which occur after a normal interval has followed the operation.

That anoxia as the cause of cerebral damage is not accepted unequivocally is attested by the number of cases reported in which causes other than anoxia are given for various sequelae of anesthesia. This is probably as it should be, for it is apparent in reading large series of articles that authors are often so engrossed in riding a special hobby, propounding a favorite theory, or expounding the merits of certain drugs or methods that they are carried away from the real import of the events which they are recording. Because of the recent emphasis on anoxia, it requires courage to mention factors other than anoxia in reporting unusual postoperative complications.

Edwards and Warrick[35] (1947) cautioned against overemphasis of anoxia. "True coma may occur after an anaesthetic in which anoxia has been present. . . . It is necessary to recognize the occasional occurrence of functional cases, as energetic physical treatment, so important in the curable cases of organic lesions, is likely to do the patient more harm than good."

An incident reported by Belinkoff[11] (1949) illustrates this point. A child, aged 5, was given avertin and ether-oxygen in preparation for bronchography. A convulsion preceded the operation. It was relieved by 4 cc. of 2½ per cent pentothal sodium. One hour and forty minutes later she seemed to be awake but was screaming and throwing her head against the pillow. "This was of great concern to the attending physicians, who thought her condition resembled that of a decerebrate and permanent brain damage from the convulsion and associated anoxia might have occurred. However, reassurance from the nurses and family that this was merely the reaction of a spoiled child led [the physicians] to leave her completely alone. After several hours of studious neglect, she quieted down to normal. Her family stated that she was perfectly normal and that they could notice no personality changes."

Another case in point is that of Hirshfeld[75] (1941): "It is only quite recently that attention has been focused on cerebral damage from anesthesia as a possible cause of post-operative mortality. Before the anesthetic itself can be denounced as the cause of post-surgical coma, the more common renal, metabolic and pulmonary

complications must be excluded. . . ." In a case of coma following a period of respiratory arrest during nitrous oxide-oxygen anesthesia, aminophylline was administered after other therapeutic measures had failed to rouse the patient. "Forty-eight hours after the institution of therapy, she responded rationally to conversation. . . . The patient went on to an uneventful recovery. No neurological or cerebral sequelae manifested themselves after the disappearance of the coma. . . . Seven weeks after operation, the patient was completely symptom-free and revealed no sign of any cerebral damage."

Adams[3a] in 1894 concluded that *idiosyncrasy to nitrous oxide* was the cause of a death. The brain did not reveal abnormalities of the cerebral substance. *Status thymicolymphaticus* (Davies[27]), *thymus* (Owens[115]), *status epilepticus* (Healy[71]), *chronic encephalitis* (Ginker and Walker[62]), *carotid sinus* (Downs[31]), and *acidosis* (Ross[125]) are among the causes ascribed by the authors to episodes that might well be placed in the category of anoxic phenomena. Uremia, senility, diabetes, and other diagnoses have been made in cases of postoperative coma and psychosis.

As the concept of cerebral damage from anoxia became clearer, there began to appear a series of reports discussing the phenomena, experiments specifically designed to study them, and reports of cases. Cases previously reported were reclassified. From the time of Courville's monograph in 1936, in which he reported incidents accompanying nitrous oxide anesthesia, reports have been made that incriminate most of the anesthetic agents being used.

A chronological listing of these reports is made to show the development of the concept. Articles are reported here without attempt to categorize them according to anesthetic agent or to separate discussions from case reports. Pertinent comments were often included with case reports. Since some of the cases of convulsions during anesthesia present a clinical picture comparable to those classified under anoxic sequelae, these have also been included in this sequence.

Among the early reports is one case which may have been the result of oxygen deprivation. Stanley[137] (1842) reported a case in which, after ten inspirations of nitrous oxide, a young man experienced only slight effect. He again breathed gas, and a series of violent muscular motions resulted which lasted for ten minutes. Alternate violent muscular exertions and intermissions continued for one half hour. He recovered in a day or two during which he had throbbing sensations in the forehead. Stanley reasoned that impure gas had been made and was the cause of the difficulty.

Ashford[4] (1869) reported an incident in which a young woman was unconscious for two hours following nitrous oxide anesthesia for a dental extraction. Headache persisted but the patient started for home. She became faint and dizzy and recalled nothing further until the following day when she found her left arm useless. Pain in her head continued, and at times she was delirious. There were motor and sensory changes involving the left part of the face, tongue, and upper and lower extremities. Later typhoid fever developed. The patient recovered. The author questioned whether the nitrous oxide might have produced "congestion

of the brain and diffusion into its ventricles or tissues," or whether this case might verify the truth of the contention that "typhoid fever is essentially a nervous fever." Four months after the anesthetic the patient walked with ease, her face was unaffected, and headache had disappeared.

Warner[149] (1882) reported a case of twitching at the right angle of the mouth and of the hand of a patient during nitrous oxide anesthesia for dental extraction. The patient regained consciousness quickly.

Buxton[14] (1887), experimenting on human beings to determine the cause of ankle clonus during nitrous oxide anesthesia, concluded that: "Whatever view we adopt with regard to ankle clonus, we have to further explain how, under nitrous oxide the cerebral-spinal axis, the peripheral nerves, or the muscles, become so altered that this phenomena can appear and vanish with recovery from brief narcosis. . . . Rhythmic jactitations attend nitrous oxide administration in a certain number of cases. The clonic and tonic contractions, it should be observed, so occurring are quite different from the irregular convulsions, the result of stimulation, brought about by asphyxia. . . . Ankle-clonus . . . is dependent upon changes, probably of an irritative character, occurring in hypertonic muscle, and brought about by like changes in the whole nervous system."

Savage[128] (1887) discussed postoperative insanities. He outlined the course of the disorder in the following manner: "Any cause which will give rise to delirium may set up a more chronic form of mental disorder quite apart from any febrile disturbance. (a) The most common form of mental disorder which comes on in such cases is of the type of acute delirious mania; (b) though such mental disorder is generally of a temporary character, it may pass into a chronic weak-mindedness, or it may pass into (c) progressive dementia which cannot be distinguished from general paralysis of the insane." In addition he reported that he had seen cases of insanity after all anesthetics. He reported five cases, three of which could probably be included in the group under consideration:

Case 1.—A man, aged 26, with a family history that included nervousness and insanity and who had an alcoholic tendency, developed an acute mania. He was given chloroform for examination of an injured hand. An acute manic episode followed his recovery from anesthesia. He recovered.

Case 2.—A woman, aged 21, with an acquired neurosis had had one acute maniacal episode from which she recovered. Chloroform was administered for an examination. Acute insanity followed.

Case 3.—An elderly man was given an ether anesthetic during which no unusual episode occurred. When he recovered, his mind was affected. He acted "half-drunk." He eventually recovered and became mentally alert.

Case 4.—A young woman, after transfusion and stimulants after the birth of a child ten years previously, had developed hysterical attacks and a tendency to use alcohol excessively. She had had one acute attack of dementia. Nitrous oxide was given for dental extraction. A maniacal outbreak followed the recovery. She never regained her senses or recognized her friends. She became "silly and fat."

Case 5.—A woman was anesthe-

tized (agent was not mentioned) for removal of a simple breast tumor. "At once after the operation she was noticed to be changed in character, irritable and exacting, unstable, with weakened control and loss of memory." Tremors, hesitant speech, defective memory, and unequal pupils persisted until death five months later. The postmortem examination showed "wasting of brain, with excessive fluid, adhesions of membranes to the cortex." The author mentioned that another such patient was under his care.

Homans[74] (1889) reported two cases of dementia following ether anesthesia for amputation of the breast, the patients being ages 35 and 50. The symptoms in each patient were the same. After operation a period of "euthanasia" existed for two days; on the third day the patients became excited; the mind wandered. This state persisted until the fifth day when it appeared that the "mind was gone." Excited babbling and delirium lasted for one week. Both patients were "well mentally thereafter." Both were from nervous families.

Gorton[58] (1889-90) reported two cases. A boy, aged 14, of good mental capacity became maniacal following tardy recovery from ether which was administered for extraction of teeth. There had been no episode of unusual nature during the course of anesthesia. Later it was reported that he "did not appear like himself." Eventually he became somewhat "demented." The second case was of a woman, aged 22, of good intelligence. Ether was administered for dental extraction. More than two hours elapsed before she recovered. After wakening she became dull and indifferent. Later she became irritable, self conscious, and "dramatic" in her actions. Fourteen months later she became hysterical and maniacal. This acute phase gradually subsided.

De Forest[29] (1897) reported the case of a woman, aged 51, who was given ether for the removal of a lump from the breast. The evening after operation the left arm and leg could not be used. She could speak only with difficulty. She became progressively worse until death on the sixth day. The rectal temperature rose to 103 F.

Garrigues[47] (1897) in discussing paralyses that followed anesthesia reported four cases of lameness. He said: "Anaesthesia-paralysis of central origin is much rarer than that of peripheral origin and is rather obscure. It may be due to cerebral apoplexy or emboli; either of which would produce ischaemia in the surroundings and secondary softening of the brain." He mentioned the case of an old woman who was given chloroform for one hour. Acute mania followed. The author recommended avoidance of operation on the aged and avoidance of prolonged operation to prevent this complication.

Green[60] (1901) reported an incident in which gas was administered, using Barth's inhaler and allowing plenty of air. A few minutes after the patient recovered consciousness, numbness of the hands, legs, and feet was experienced. The hands were pronated, the fingers slightly flexed, and the thumb adducted. Respirations were rapid and stridorous. His color was excellent; he was restless and unable to articulate. These symptoms continued for more than twenty minutes. The man was not hysterical.

Lamb[88] (1903) reported a case of respiratory arrest during chloro-

form anesthesia lasting one and one-fourth hours. An "intracranial condition being suspected," and a trephine exploration of the cerebellum was made with negative findings. The patient began to breathe after vigorous treatment including tracheotomy and galvanic current. The respiratory arrest recurred thirty hours later. The postmortem examination disclosed a "small cerebellar abscess."

Gabriel[45] (1905) reported a case of paralysis of the soft palate with swallowing difficulty following nitrous oxide anesthesia.

East[33] (1908) recorded a case of a patient, aged 21, with no history of previous mental instability who was given ether for forty minutes for extraction of teeth. Mania immediately upon recovery was followed by sleep. Upon awakening the maniacal state recurred. The temperature was elevated to 102 F. On the fourth day after the episode, he was quieter. Recovery was uneventful.

Ross[125] (1921), in discussing acidosis following operation, briefly outlined the clinical picture presented by these patients "which varies in severity from those showing rather prolonged nausea and vomiting, headache, and slight restlessness, to those cases in which the patient rouses from the anesthetic only to lapse into a rapidly deepening coma, with rising temperature, pulse and respiration rates and with death supervening within twenty-four to forty-eight hours."

Caine[17] (1932) reported four cases, one patient dying on the operating table. Three survived for varying periods. A woman, aged 39, became apneic during nitrous oxide anesthesia. The saturation technic was used. Cardiac failure occurred; resustitative measures produced resumption of cardiac and respiratory function. The patient responded without regaining full consciousness but died during the first day. A second patient, a woman, aged 58, was anesthetized by the saturation technic with nitrous oxide and oxygen. Cardiac failure was overcome by cardiac massage. She recovered six hours after operation. Visual disturbances, vomiting, and restlessness were present. The course was progressively downward until her death two months later. The third case was of a woman, aged 37, in whom respiratory and cardiac failure occurred during a laparotomy under nitrous oxide-oxygen-ether anesthesia. After three years she could speak unintelligibly; blindness and paralysis persisted beyond six years. In commenting on these cases the author said: "Restoration of the heart's action and respiration does not mean that the patient is all right, but there are likely to be degenerative changes in the brain that are irreparable. Restoration of consciousness and apparent normality after the heart has stopped under these circumstances does not mean that there is no permanent damage to the brain that will be manifested later. The human brain cannot stand the suspension of circulation and return to normal as can the brain of the dog."

Atkeisson[5] (1923) reported one case of a woman, aged 25, who was anesthetized with nitrous oxide and oxygen for an examination six weeks after an accident and delivery of a premature baby. During the course of anesthesia, respiration ceased for fifteen minutes. She wakened in delirium and remained incoherent, mumbling, and crying until death twenty-four hours later. Examination of the brain was not done.

McCardie and Featherstone[98] (1926) reported two incidents that occurred in the same operating room, the patients dying within an hour of each other. The first was a woman, aged 60, who was given E_2C_1 mixture with a "little ethyl chloride" for amputation of a breast. After twenty-five minutes of anesthesia, respiration ceased. Respirations became spontaneous fifteen minutes later. She did not recover from the anesthetic and died twenty hours later without regaining consciousness. The temperature was 106 F. Postmortem examination showed cerebral softening—thrombosis of basilar arteries and the sylvan arteries. Metastasic lesions and recent hemorrhage involved the right half of the cerebellum. The second patient, a man, aged 48, was anesthetized following perforation of a duodenal ulcer. E_2C_1 mixture was used for the induction during which the patient struggled for four minutes. Oxygen was administered because of cyanosis. Twenty minutes after induction the color was improved, but the respirations were jerky and then ceased. Heart action ceased. Artificial respiration, cardiac massage, and intraventricular injection of adrenalin resulted in return of cardiac and respiratory function three or four minutes later. Respirations remained spasmodic for an hour and twenty minutes. Diagnosis of hemorrhage in the area of the pons varolii was made. Death occurred five and one-half hours after restoration of respiration. Postmortem examination showed the brain to be edematous; vessels of the pons and the floor of the sylvian aqueduct were congested.

Glynn[56] (1926) reported one case: "An apparently healthy lad was anaesthetized with nitrous oxide and the stump of a molar tooth extracted. He never recovered consciousness and died in thirty-seven hours. . . . The administration of the anaesthetic and the extraction took a minute, or slightly more. The patient began to recover, . . . but soon went 'nasty color, then black' and collapsed. [Convulsions began several hours later. The necropsy revealed that] the brain was congested and contained a few punctiform hemorrhages; . . . the lungs showed moderately extensive lobar pneumonia."

Clement[18] (1928) reported three cases in which convulsions followed periods of anoxemia after anesthesia. He advanced the opinion that so-called ether convulsions are probably due to anoxemia. A young man had convulsions after an anesthetic of nitrous oxide, ethylene, and oxygen. Percentage of oxygen had been low (4-6 per cent). He recovered. A child, aged 7, had convulsions during anesthesia; oxygen was given, and the child recovered. A child had convulsions during nitrous oxide anesthesia; frequent additions of oxygen controlled the convulsions, but at the close of the procedure, in spite of oxygen, convulsions became so severe as to interfere with breathing. Bromides and atropine were administered; the child recovered.

Evans[38] (1928) reported seventeen cases of anoxemia in which inhalations of oxygen overcame the difficulties except in three of the patients who did not recover.

Weber[151] (1931) reported a case of a boy, aged 14, who could not see or hear in a conscious way. A diagnosis of decerebrate automatism was made. At the age of 2 years the child had convulsions during ether anesthesia given for appendectomy. The child had been normal before

the operation. The convulsions lasted for twenty hours and thereafter occurred at frequent intervals. In commenting on this case the author said: "It seems as if the nerve cells of the whole cerebral cortex that are concerned in the voluntary movements and conscious perception of all kinds have been selectively destroyed in a way analogous to that in which the glandular cells of the whole liver have sometimes been more or less selectively destroyed in cases of acute hepatic atrophy following chloroform anaesthesia. It is just possible that, with the convulsions there may have been a diffuse bilateral sudden haemorrhage to the cerebral cortex."

Yaskin[162] (1931) recorded an incident in which "immediately after an instrumental delivery a previously healthy woman presented an acute and diffuse involvement of many regions of the brain, particularly striking was the involvement of the supranuclear structures concerned with articulation and swallowing, disturbances of consciousness, transient blindness, general increased tonus in the musculature with increased reflexes, myoclonic movements of the extremities and transient weakness of the extra-ocular muscles. These phenomena were accompanied by a febrile course and a serious constitutional reaction with no evidence of meningitis. There followed a rapid recession of symptoms with residues pointing to a slight but permanent damage to the extrapyramidal system." Nitrous oxide was used. The baby appeared normal in color.

Landau and Wooley[89] (1934) reported a case in which restlessness, giddiness, spots before the eyes, and photophobia followed evipal gas-oxygen anesthesia. On the fifth day headache, nystagmus, and vomiting developed. The symptoms cleared on the eighth day, and recovery thereafter was uninterrupted.

Quastel[119] (1934) studied the effects of oxygen deficiencies and remarked that "the similarity between the psychological reactions following oxygen want and those found in light narcosis, and the resemblance of these to the reactions found in certain types of mental disorders have attracted a number of investigators. It has become a likely hypothesis that certain forms of mental disorders may find their origin in a physiological state corresponding to anoxaemia."

Lennox et al[92] (1935) concluded: "Neither sleep nor epileptic seizures are due to reduction in the total cerebral circulation. . . . In man unconsciousness supervenes if the oxygen supply to the brain is suddenly reduced to such an extent that the oxygen saturation of the blood in the internal jugular vein falls to 24 per cent or below."

Courville[20,22] (1936) (1939) reported thirteen cases, in nine of which the condition was fatal. The case summaries are quoted:

"Case 1. Exploration for interlobar pulmonary abscess under nitrous oxide-oxygen anesthesia. Period of irrationality, lethargy and aphasia with signs pointing to lesion of left frontal lobe. Recovery. Re-exploration two years later under nitrous oxide-oxygen anesthesia with marked cyanosis. Generalized convulsions, continuous stupor and death. Survival period 40 hours."

* * *

"Case 2. Nitrous oxide-oxygen anesthesia for delivery and perineal repair. Respiratory failure under anesthetic. Generalized convulsions, muscular twitchings and deepening coma. Death after 43 hours."

"Case 3. Convulsive seizures and coma following administration of nitrous oxide anesthesia for extraction of teeth. Death after two and a half days."

* * *

"Case 4. Nitrous oxide-oxygen anesthesia for biopsy of nodules in old scar at site of mastectomy. Cyanosis and cardio-respiratory failure. Generalized convulsions. Death after three days."

* * *

"Case 5. Respiratory failure under nitrous oxide-oxygen anesthesia for curettage of chronic osteomyelitic focus of right tibia. Residual coma and generalized muscular twitching with decerebrate rigidity. Death after four days and seven hours."

* * *

"Case 6. Administration of nitrous oxide-oxygen supplementing spinal anesthesia for hysterectomy. Continued coma. Diffuse minor motor manifestations. Survival period 5 days."

* * *

"Case 7. Nitrous oxide-oxygen-ether anesthesia for perineorrhaphy and repair after normal delivery. Irregular respiratory movements without cyanosis during anesthesia. Localized and generalized convulsions and coma. Temporary improvement followed by decline and death. Survival period 6½ days."

* * *

"Case 8. Respiratory irregularities under nitrous oxide-oxygen anesthesia for curettage of the uterus. Coma followed by delirium. Septicemia. Death 19 days later."

* * *

"Case 9. Extraction of teeth under nitrous oxide-oxygen anesthesia. Transient respiratory failure followed by convulsions and coma for 24 hours. Improvement in mental status for several days. Complete blindness followed by deep coma and death in 26 days after onset."

* * *

"Case 10. Nitrous oxide anesthesia for resection of fallopian tube (ectopic pregnancy). Incomplete recovery with residual parkinsonian syndrome. Survival with mental defect. Committed to a mental hospital."

* * *

"Case 11. Residual lenticular syndrome in a patient surviving an anoxemic episode after nitrous oxide anesthesia eight years before."

* * *

"Case 12. Nitrous oxide-oxygen-ether anesthesia for repair of perineal laceration after precipitate delivery. Cyanosis and respiratory failure. Generalized convulsions followed by state of restless delirium. Recovery after transient aphasia, apraxia and visual disturbances."

* * *

"Case 13. Cyanosis and muscular rigidity during short nitrous oxide anesthesia for curettement. Twenty-four hour period of restlessness. Respiratory irregularity and vomiting. Complete recovery."

A review of the subject of asphyxia following nitrous oxide anesthesia, extensive discussion of the pathologic changes in the brain, and case histories make up a monograph of which the summary is quoted here:

"This study is concerned with the problem of cerebral asphyxia or anoxia as a result of nitrous oxide anesthesia. It is based upon clinical and pathologic observations in a series of 13 cases, 9 of which terminated fatally. In all the fatal cases an autopsy was obtained and

a more or less critical examination of the cerebral tissues was made.

"Cerebral manifestations following inhalation of nitrous oxide have been recognized for almost a hundred years. The immediate nervous manifestations usually consist of generalized convulsive seizures, muscular rigidity and persistent coma, at times terminating fatally with signs of 'decereberate rigidity.' Delayed symptoms may occur in the form of a psychosis, a parkinsonian symptom-complex or disturbances of special sensation, particularly in the form of a partial or complete amaurosis. The patient may recover entirely after an anoxemic episode, may survive for a variable period with residual symptoms or may die within a few days. In fatal cases, death usually occurs within 2 to 7 days, but may occur only after an interval of weeks or months. Examples of each of these variations are to be found in the series of cases described herewith.

"Anoxemia following administration of nitrous oxide may be the result of an impure gas, a faulty apparatus, or a preëxisting or suddenly developed pulmonary lesion. The possibility of faulty administration of the anesthetic and of individual idiosyncracy to this gas are also to be considered. Several factors may be present in a single case, all contributing to production of the cerebral lesion. Regardless of the exact source of the trouble, the clinical symptoms and the pathologic findings are the effect of *asphyxia* and are not due to any toxic effect of nitrous oxide itself.

"The mechanism in most instances seems to be one of two types,—*(a)* sudden circulatory and/or respiratory failure with consequent cerebral damage due to the immediate utilization of the remaining small amounts of available oxygen or *(b)* prolonged exposure of the brain to a dangerous degree of oxygen want.

"The resulting cortical lesion necessarily depends upon the degree of anoxemia and its duration. There may be *(a)* a sclerosis of scattered pyramidal cells, *(b)* an occurrence of discrete pale areas (*Herde*) in the cortex, *(c)* a patchy necrosis of superficial, intermediate or deep, or all cortical layers, *(d)* a subtotal destruction of the cortex, or if the patient survives for a sufficient interval, *(e)* a vascular scar may result due to the formation of new blood vessels. Changes in the nerve cells may be described as *(a)* sclerotic, *(b)* acute degenerative, *(c)* ischemic, and in chronic cases *(d)* 'calcified' nerve cells. Lipoidal degeneration *(e)* is also a common form of cellular change. The microglia develop into compound granular corpuscles in the presence of necrosis. The astrocytes adjacent to the necrotic areas undergo proliferation to aid in the formation of the astro-vascular scar. The oligodendroglia undergo acute swelling and variable degrees of proliferation, particularly in the subcortical white substance. The arachnoid and pia may show cellular proliferation, and adhesions between these two membranes may take place.

"The lenticular nucleus seems to be affected to about the same degree as the cerebral cortex, and essentially the same architectural and cellular changes are found. Small globules of calcium are commonly observed in the small blood vessels in this structure similar to those found in carbon monoxide poisoning. The Purkinje cells of the cerebellar cortex are quite markedly altered.

"A study of the brain in fatal cases discloses several interesting facts. Not all portions of the cortex are uniformly or symmetrically involved. This no doubt explains the variable clinical picture found in those cases surviving for several weeks or more. While it is possible to predicate the character of the lesion from the clinical history, one cannot always be sure of the severity of cortical damage. This is due to the great difficulty in evaluating all the possible causative factors. The earliest lesions are found about the pericellular and pericapillary spaces, which would suggest that the injury is a result of 'tissue respiration',—a disturbed carbon dioxide-oxygen exchange between the tissue fluids and the cellular elements.

"This condition, hitherto not critically studied from a clinical and pathologic standpoint, demands further investigation. A careful analysis of all possible factors should be made at the time an accident occurs under nitrous oxide anesthesia to determine if possible the cause of the trouble. A detailed study of the brain should be made in every fatal case. The ultimate changes taking place in the brain after prolonged survival period are as yet unknown."

Courville[21] (1936) reported on one of the cases from his previous study in which the patient with residual lenticular syndrome continued to improve three years after the former report.

Lowenberg et al[95,96] (1936) (1938) reported three cases of cerebral cortical and basal ganglion destruction and an additional case in which clinical evidence of a similar process was apparent. In one case after ten minutes of respiratory arrest rigidity and tremor occurred. Continued unconsciousness, pyrexia, loss of tendon reflexes, rigidity, and tremor progressed until death sixty hours after the onset. Necropsy disclosed severe injury of the cerebral cortex, basal ganglion, and midbrain. A second patient, in whom respiratory arrest occurred during nitrous oxide anesthesia, died seventy-two hours after the episode. Examination of the brain showed severe damage of the cerebral cortex and basal ganglions. In case 3 cardiac and respiratory arrest occurred after one hour of nitrous oxide anesthesia. Pyrexia, twitchings of the left hand, rigidity, and coma lasted until death 119 hours later. The brain showed damage similar to that in the preceding cases. The fourth patient had similar symptoms several hours after operation. He recovered. Six and one-half years later there were signs of residual neurologic damage. There was no impairment of mentality. The author's comment was: "The histologic picture suggested that the destruction of the brain is due to the toxic action of nitrous oxide on the parenchyma. A definite selective destruction is noted, the cortex and the basal ganglion being much more severely damaged than the brain stem and the cerebellum, resulting in a clinical picture of decortification. Destruction of this type is frequently a toxic manifestation and similar findings have been noted in the cases of poisoning by excessive doses of pantopon, morphine, and ergoapiol. Therefore, death may be due to extensive destruction of the cortex and basal ganglia rather than to involvement of the respiratory area per se."

Ford et al[44] (1937) reported one case of extensive injury to the cerebral cortex.

O'Brien and Steegman[113] (1938)

reported one case in which death occurred sixteen months after the administration of nitrous oxide anesthesia. During those months there was never a return to the conscious type of mental activity. Marked degenerative changes in the brain were evident.

Gebauer and Coleman[48] (1938): A woman, aged 29, was anesthetized with cyclopropane by the carbon dioxide absorption technic for two hours and thirty-five minutes. Moderate shock developed. She was stuporous four hours after operation. Thirty-six hours postoperatively mild convulsions, coma, and cyanosis developed. There were no definite neurologic findings. Muscle rigidity was apparent on the fifth day. She remained unconscious until death on the seventh postoperative day. Autopsy showed "extensive degenerative process of the cerebral cortex."

Abbott and Courville[2] (1938) reported an episode in which a woman, aged 37, was given nitrous oxide and oxygen for fifteen minutes, then ethylene, oxygen, and ether. There was marked cyanosis at the time the anesthetic agents were changed, and irregular respirations for the remaining forty-five minutes. Very little ethylene was given. Coma persisted for two days postoperatively. Retardation of voluntary speech, frontal headache, faintness, and disorientation developed later. She died on the forty-second day. Following autopsy the authors commented it seemed that the "globus pallidus of the lenticular nuclei is the most sensitive part of the brain to the effects of asphyxia."

Stewart[139] (1938) presented a case "in which apnea occurred during nitrous-oxide and oxygen anesthesia, causing widespread destruction of the nerve cells of the cerebrum. Neurologic symptoms appeared within an hour and lasted about forty-eight hours, when coma supervened. Death from pneumonia occurred on the thirteenth postoperative day. . . . Autopsy showed changes in the cerebral nerve cells similar to those found after experimental cerebral hypoxemia, and to those described in other cases of asphyxial death after nitrous-oxide and oxygen anesthesia and poison from illuminating gas and automobile exhaust gas."

Griffith[61] (1938) reported an incident in which a 14 year old boy was given cyclopropane anesthesia. After induction and intubation a pack soaked in 2 per cent nupercaine was placed in the nose. Forty minutes later convulsive actions of the hands were noted. Anesthesia was deepened. Later tetanic spasms involving the head, face, and neck developed. Respirations were depressed. The laryngeal reflex did not return promptly. After prolonged sleep recovery was uneventful.

Courville[23] (1938) reported the effects of asphyxia on the cerebral gray matter following nitrous oxide anesthesia.

Gitlin[55] (1938), in reporting a case of convulsions that occurred during nitrous oxide anesthesia, mentioned the development of headache as a sequel to the convulsion.

Schreiber[132] (1939), in discussing the subject of cerebral anoxia, said: "Cases recorded in the literature with the diagnosis of 'liver death' would seem, on closer scrutiny, to be more properly classified as examples of cerebral anoxia. . . . The author has had occasion to observe several hundred individuals who exhibited evidence of disturbed cerebral architecture,

probably as a result of an asphyxial episode associated with the administration of an anesthetic agent. Some of these patients had been given a general, spinal or local anesthetic for relief of pain during a surgical procedure. Others had been anesthetized through the placental circulation, the mother receiving anesthesia to abolish the pain of childbearing. Most of the cases in which severe neurological symptoms appeared following anesthesia were thought to fall into the anoxic anoxia group. . . . Unless the anesthetist can recognize cerebral asphyxia in the absence of cyanosis and remedy the situation, the consequences may be grave. . . . While the neuropathologist can report only what he sees under the microscope, it is most significant that in those cases in which death has been delayed a few hours or more following nitrous oxide asphyxia, there can be demonstrated a diffuse degeneration of the brain tissue. The determination of the etiology of this brain change must be left to the clinician who observes these cases while still living and is familiar with all the circumstances of the individual case. . . . A catabolic type of anoxic anoxia also plays an important part in cerebral alterations associated with anesthesia. Although the oxygen supply may be normal, intrinsic or extrinsic factors may increase the demand of the tissues to the point where this demand cannot be fulfilled. In these cases, drugs which depress the respiratory mechanism are thought to inhibit the integration between increased oxygen demand and the available oxygen supply. . . . For every degree of fever there is a corresponding increase of at least 7 per cent in oxygen demand. Several of the cases under discussion were children with high temperatures at the time of operation who began having generalized convulsions immediately following operation or on the operating table during nitrous oxide-oxygen-ether or ether anesthesia. . . . It is of utmost importance to keep up the blood volume during operative procedures in order to avoid anoxic brain changes. In the integration necessary for adaptation to lowered blood volume and anemia . . . the amount of oxygen supplied with the anesthetic must be increased to meet the changing conditions in the patient's internal environment or cerebral tissue will succumb. . . . Excessive preoperative medication may set the stage for cerebral anoxia because the respiratory and cardiac centers, depressed by drugs, cannot function properly to meet varying oxygen demands of cerebral tissue during anesthesia. . . . Any imbalance in the neurohumoral chemistry of cerebral cells must be taken into account. . . . Dehydration, hypoglycemia or hyperglycemia, deficiencies in calcium, potassium, or phosphorus can inhibit the ability of the cell to utilize oxygen and in this way initiate a destructive anoxia. . . . In 5 patients with cerebral changes following spinal anesthesia, . . . large doses of pre-operative medication had been given in each instance. . . . It appears that in rare cases even local anesthesia may set up a histotoxic anoxia, leaving cerebral devastation in its wake."

Steegman[138] (1939) reported four cases, in the first of which a man, aged 37, was given avertin (100 mg. per kg.) in preparation for encephalography. Collapse was followed by a twenty-four hour period of restlessness. Spasticity developed. He remained unconscious until death ninety-six hours after the episode. Extensive diffuse defects and degenerative

changes in the ganglion cells, proliferative reaction of the neuroglia, and cells in a state of dissolution were reported after autopsy. The second case had previously been reported (Gebauer and Coleman[48]). The third, a man, aged 30, received nitrous oxide and oxygen anesthesia for repair of an injury of a finger. After a few breaths of pure nitrous oxide, cyanosis developed. Oxygen 12 per cent, then 20 per cent, did not improve the color. A small amount of ether was given. Respiratory arrest ensued. This was corrected by artificial respiration. Consciousness was regained slowly. Convulsions and clouded sensorium were apparent upon recovery. On the second postoperative day the patient became noisy and restless; the third day visual disturbances were noted. The patient left the hospital on the fourth day, apparently normal. Tremor and convulsions returned. On the fifth day spastic gait, hypertonicity of the left arm and leg, and progressive paralysis developed. He became stuporous and restless, and twitchings were noted until death on the twelfth postoperative day. Examination of the brain showed a degenerative process. The fourth case had previously been reported (O'Brien and Steegman[113]).

McClure et al[101] (1939) reported four cases. Case 1.—Following an anoxic episode, the patient died in the operating room. Case 2.—Following an operation which lasted three and one-half hours, the patient continued in a drowsy state. Speech and swallowing difficulties were noticed as well as left facial paralysis and mental confusion. The anesthetic was not specified. The patient was "discharged." Case 3.—Avertin, nitrous oxide-oxygen were administered following which the patient remained unconscious for five days; later he was mentally confused. Case 4.—Following ethylene-oxygen-ether anesthesia a patient did not regain consciousness. Four and one-half months later the speech was unintelligible and hemiplegia persisted.

Dawkins[28] (1940) reported 2,406 anesthesias with vinethene of which nine were attended by convulsions, none fatal. Of 196 in-patients, four had convulsions. Of 2,210 out-patients, five had convulsions. The in-patients had convulsions similar to those seen with deep ether anesthesia during the close of operations. The out-patients were children between the ages of 3 and 9, and in each instance the convulsions came on "after the anesthetic was concluded. Anesthesia was normal in each case and the child was then removed to the recovery room, where it recovered consciousness sufficiently to start spitting out, twitching of the facial muscles then began, and soon all the muscles of the body were involved. The child would then become unconscious and cyanosed, and would cease breathing. . . . Artificial respiration was employed and preparations were made to give evipan; but in each case respiration restarted before evipan was given, and the convulsions gradually ceased. The colour returned to normal and the child would then sleep for about an hour. If awakened before this it would get up and run about the room, banging its head on the walls and appearing completely incoordinated. . . . Those who were allowed to sleep during the cessation of convulsions awoke normally in about an hour. . . . The mental symptoms would appear to indicate some form of cerebral damage, fortunately not of a permanent nature."

Batten and Courville[9] (1940) re-

ported ten cases, the first five having been previously reported.

Case 6.—A woman, aged 27, was delivered of a normal child under nitrous oxide and oxygen anesthesia. She remained unconscious for thirty-five hours. During this period she talked and repeatedly asked about the condition of her child. When consciousness returned she had blurring in the left visual field, thickness of speech, difficulty in swallowing, jerking movements of both arms, and marked paresis of all extremities. These symptoms persisted for one month. During the next three months she was easily fatigued, emotionally unstable, had a feeling of inadequacy, and loss of interest in her work, social contacts, and music. Her memory was poor, and it was difficult for her to concentrate. Three years later she was still somewhat unstable; when fatigued her hands were unsteady; her interests in avocations had not entirely returned. "This 'flattening of the emotional curve' seems to be one of the persistent residual characteristics of the anoxemic states provoked by nitrous-oxide oxygen anesthesia."

Case 7.—A woman, aged 30, had a precipitate delivery. Nitrous oxide-oxygen-ether anesthesia was given for repair of a lacerated perineum. After a short period of time respirations became labored, then ceased. They were re-established within a few minutes upon administration of oxygen. She remained comatose, and convulsions, restlessness, and delirium developed. Her mental condition improved. Examination four days after the episode found her rational; there were apraxia of the right hand and limitation of vision to the lower quadrants of the visual fields. Five weeks later she appeared to be perfectly normal. "The period of respiratory failure was very short and this probably accounts for the lack of permanent mental symptoms."

Case 8.—A woman, aged 28, following an incomplete abortion, had a dilatation and curettage done under nitrous oxide-oxygen anesthesia. Cyanosis and rigidity developed, but there were no cardiac or respiratory irregularities. When she was removed from operating table, she screamed in a hysterical manner. This continued until she was quieted with paraldehyde. One hour later restless stupor and purposeless movements of the extremities developed. She could not be aroused. Later in the day she became quieter. The next day she seemed quite normal mentally. Nine days later there were no residual symptoms. "The peculiar staring silent gaze . . . seems to be one of the immediate residual characteristics of the condition."

Case 9.—A woman, aged 26, whose hemoglobin was 50 per cent, did not recover promptly following nitrous oxide-oxygen anesthesia. She appeared to be very dull, unable to comprehend, would sit upright in bed staring wide-eyed, and ask questions in an idiotic manner. She appeared to be distressed mentally, moaned, and moved her arms in an aimless manner. Oxygen inhalations and transfusion were given, and she became quiet. The next morning she was somewhat obtuse mentally but understood what was said to her and talked in a rational manner. There was amnesia for events of the previous day. From then on there was an uneventful postanesthetic course. She was perfectly normal mentally fourteen days later.

Case 10.—A boy, aged 5, had eight teeth removed under nitrous

oxide-oxygen anesthesia. He was never cyanotic but once "caught his breath." He slept for two hours and when roused cried out in a hysterical manner. He did not recognize his mother. Later he cried incoherently and was unco-operative. There was advanced defect in sight and hearing. The next morning he had entirely recovered.

Monroe and Benjamin[106] (1941) reported a case of convulsions in which some of the symptoms of acute anoxia were evident. Following a convulsion that occurred after seventy-three minutes of anesthesia, the patient died on the seventh postoperative day. "A neurological examination . . . was made 36 hours after the onset of convulsions. The patient was in profound stupor, there was no response to pin pricks. The ankle jerks were present and about equal; the knee jerks were present and very brisk. . . . No pathologic reflexes were present. The cremasteric and abdominal reflexes were absent. No facial asymmetry was present; the patient did not respond to external stimuli. . . . Necropsy was performed four hours after death. . . . The essential anatomic diagnosis was: Bilateral confluent broncho-pneumonia; unresolved pneumonia with beginning carnification; necrotic hemorrhagic infarct of the left upper pulmonary lobe; pulmonary thrombosis; dilatation of the right heart; mild diffuse hemorrhages of the pia-arachnoid; edema and perivascular hemorrhages of the brain; hypoplasia of the aorta; involution of the thymus; atrophy of thyroid. . . . The severe generalized ganglion-cell degeneration found as a result of heat stroke or hyperthermia was not observed."

Courville[24] (1941) studied cerebral anoxia and ether anesthesia. He reported two cases and commented: "The relatively high mortality of cases with ether convulsions . . . about 18% . . . clearly indicates that we are not dealing with an ordinary convulsive state but one symptomatic of a more lethal background. . . . More to the point in the possible connection of ether complications with true asphyxia are those instances in which death is delayed for a variable interval of time, or in which permanent or transitory neurologic or psychiatric manifestations betoken serious or minor disturbances of the gray matter of the brain. . . . Case 1, Ethyl chloride ether anesthesia. . . . Cyanosis and cardiac failure under anesthesia, successful resuscitation but persistent coma after operation, decerebrate rigidity and blindness as residuals. Alive, completely blind, and spastic ten months later. . . . Case 2, Ether anesthesia. . . . Respiratory failure necessitating artificial respiration and administration of stimulants. Recovery followed by psychosis and spasticity. Gradual recovery, death two years later of alcoholism."

Johnston[82] (1941) reported five cases in one of which a man, aged 40, who died seven hours after operation (anesthetic agent was not reported) had symptoms suggestive of cerebral damage.

Schnedorf et al[130] reported two cases and experiments on two dogs and reviewed the literature. The first of the cases was of a man, aged 58, who was given 100 mg. procaine hydrochloride and 5 mg. pontocaine intraspinally in the third lumbar space. Anesthesia was to the fourth thoracic level. Anesthesia was supplemented with inhalations of nitrous oxide and oxygen in a 50-50 per cent mixture. Shock developed. Blood pressure was undetectable, and respiration ceased.

With resuscitative procedures, respirations became spontaneous after twenty-five minutes. The patient reacted the following day but remained comatose for several days. He remained irrational until death twenty-one days later. Extensive cerebral damage, typical of anoxia, was shown at autopsy. The second patient was a boy, aged 3, who did not react for several hours after ether anesthesia. Lateral horizontal nystagmus and twitching of facial muscles were noted. Spasms of the upper extremities progressed to generalized convulsions, cyanosis, and death fourteen hours later. Postmortem examination showed involvement of the brain cortex and brain stem, vascularization of white matter with extravasation of blood, and degeneration of brain cells. Two dogs were subjected to conditions simulating those that existed during the anesthesias. The brains showed the same changes as those present in the patients.

Lorhan et al[94] (1941) studied the histopathologic changes in rats following administration of pentothal sodium and sulfanilamide. They found that "Sulfanilamide in doses of 0.6 to 1.0 Gm. per Kg. produces toxic effects which render white rats more susceptible to pentothal sodium. With a dosage of 1.0 Gm. per Kg. marked neurological symptoms are observed."

Ingleby et al[80] (1941) made comparative autopsy studies of eighteen dogs after anesthesia. Barbiturates, ethyl ether, and cyclopropane with oxygen were the agents used in the studies. They found that "in the brain, the cortex was most affected. Each anesthetic used caused varying degrees of Nissl's acute degeneration. In the cyclopropane-oxygen group the cerebral lesions were definitely more severe. All of this group showed some neuronophagia, the extent did not depend on the number of administrations. In interpreting these findings we consider that the acute degeneration was due to the lethal dose of the anesthetic. Neuronophagia and glial changes indicate a longer standing lesion, and are probably the consequence of previous administrations of the anesthetic. If this be so, it would indicate that cyclopropane-oxygen is definitely more toxic to nerve cells than the barbiturates or ether. When brains and livers from the first few dogs were examined it was thought that there might be some correlation between liver and brain damage. However, careful comparison of sections from the whole series showed that this was not so. . . . Two points seemed to emerge; the first is that the clinician's fear of damage to the liver as a result of anesthesia is well founded; the second is that the effects of cyclopropane-oxygen on the central nervous system will bear watching."

Turino and Merwarth[145] (1941) reported an incident in which a woman, aged 31, was given gas-oxygen anesthesia for the delivery of a stillborn baby. Ether was added to produce complete anesthesia. "As the head was being delivered with forceps . . . the patient's respiration became irregular, shallow, and slowed to less than 8 per minute. The pulse of poor quality became momentarily imperceptible, and then quickened to 144 per minute. . . . Approximately one hour following delivery of the fetus, there occurred muscular twitching of the face, first involving the left and later both sides, extreme restlessness and unintelligible jabbering sounds. The eyes remained open and staring, the pupils were dilated, and the lower

extremities were spastic. Five hours after delivery the upper extremities became rigid. The patient tossed her head from side to side, cried out loudly, and threshed around so much that restraint was necessary. The facial grimaces continued. . . . The clinical picture forty-eight hours later was that of wide-spread decortication. . . . Death occurred . . . three and one-half months after the anoxic episode. . . . Grossly scattered minute areas of necrosis were found in the gray and white matter of the cortex and the gray matter of the base of the brain. . . . Factors which may be responsible for anoxia have been traced to faulty gas machines, impurities of the gas, alcoholism on the part of the patient, or the unskilled anesthetist."

White et al[153] (1942) studied changes in brain volume during anesthesia, anoxia, and hypercapnia. Swelling of the brain occurred during exploration for an hypophyseal adenoma under local anesthesia supplemented with nitrous oxide and oxygen. Minor cyanosis produced swelling of the brain. In experiments on cats, during barbiturate or ether anesthesia, no swelling occurred when the airway was unobstructed. Anoxia, however, caused an increase in intercellular or intracellular fluid, or both.

Tye[146] (1942) reported five cases of convulsions of anesthesia with two deaths and three recoveries. One of the patients died during the convulsion; the other patient who died lived twenty-nine days in a state of decerebrate rigidity without ever regaining consciousness.

Ray and Marshall[122] reported twelve cases of convulsions that occurred during general anesthesia. The nine patients who survived showed delayed recovery from anesthesia or late sequelae, or both. The ages ranged from 2 to 44 years. Three children were given ether, six of the group received closed-mask ether with nitrous oxide-oxygen, two had ethylene-ether-oxygen, and one had cyclopropane-oxygen-ether. The authors thought that a contributing cause was the inhibition of the ability of cells of the brain to utilize oxygen. "One patient has what appears to be permanent changes in temperament and personality while another has residual hemiparesis. . . . In four of the seven patients subjected to electroencephalography at varying periods after their operations, there were pathologic changes recorded."

Suggs[142] (1943) reported a case in which a woman, aged 32, was given nitrous oxide and oxygen for fifteen minutes. The induction was "stormy." Respiratory arrest occurred although there was no cyanosis (hemoglobin 66 per cent) or pallor. Artificial respiration, oxygen inhalation, and stimulants were given. An hour elapsed before voluntary respirations returned. Three hours later spastic convulsions began; these recurred at varying intervals. Consciousness never returned. She lived in a static state for forty-one days. The postmortem examination showed "Degenerative lesions of the ganglion cells varying in severity with different regions of the cortex, being most prominent in the parietal lobes. Basal ganglia and midbrain are only moderately involved. The cerebellum reveals extensive degeneration of Purkinje cells. The Ammon's horn shows only few scattered degenerative ganglion cells."

Woodhall and Goodman[158] (1943), reporting the use of pentothal sodium in neurologic surgery, cited five cases in which complications developed, two of which are pertinent.

Case 1.—A woman, aged 23, received 2.9 Gm. pentothal sodium in seventy-five minutes for repair of median and ulnar nerves. She reacted in two hours, became maniacal for four hours. She was drowsy for twenty-four hours. "The influence of the anesthetic agent in this reaction was not clear."

Case 2.—A woman, aged 35, was given 1.45 Gm. pentothal sodium for section of the sensory root of the fifth nerve by the subtemporal approach. After recovery two hours later, she became maniacal and remained so for the next twenty-four hours.

Aageson[1] (1944) reported a case of a girl, aged 12, who was anesthetized with nitrous oxide-oxygen-ether for an appendectomy. There was normal return of consciousness. Deafness was noted two days after operation. Dizziness to the point of falling developed after the child had left the hospital. This symptom disappeared two weeks later. The deafness persisted. In commenting on the case the author said, "the lesion appears organic in nature and the outlook for further recovery seems doubtful."

Fletcher[42] (1945) reported in detail eight of twenty-nine cases that had come to his attention.

Case 1.—A woman, aged 60, had nitrous oxide administered for dental extraction at the age of 29 years. An episode of difficulty during the anesthesia had occurred. After thirty years there were apparent residual neurologic signs.

Case 2.—A woman, aged 35, a daughter of the patient previously described, had no difficulty following nitrous oxide anesthesia given for the delivery of her child. Nitrous oxide was given for short periods at ten different times for dental work. Residual signs of personality disintegration were apparent two years later. These were interpreted as the accumulated effect of many anesthetics. The occurrence of similar reactions in mother and daughter was suggestive of a predisposition to anoxia.

Case 3.—A man, aged 21, was given nitrous oxide on nineteen different occasions for dental work. One year later, residual neurologic signs were apparent.

Case 4.—A woman, aged 42, had been anesthetized for tonsillectomy at the age of 12. (The agent was not recorded.) Following the anesthesia she was lethargic for a week, and persistent headaches developed. At the age of 19, she was given chloroform during the delivery of a child. The baby was critically ill for five weeks after birth. At the age of 22, the patient had ether anesthesia, and at 24, during nitrous oxide-oxygen-ether anesthesia, she had an episode of respiratory difficulty. Several months later, residual symptoms persisted. At the age of 32, she had a nervous breakdown and psychotic signs after nitrous oxide anesthesia for dental work. At age 35, a series of nitrous oxide anesthetics were given for treatment of furuncles. There were flare-ups of the mental condition. Four times nitrous oxide was given for dental treatment with mental flare-ups after each.

Case 5.—A boy, aged 6, was given nitrous oxide-oxygen anesthesia for tonsillectomy. No untoward incident occurred. There was a decline in his mental state. Two years later he began to show marked improvement.

Case 6.—A man, aged 20, was unconscious after nitrous oxide-oxygen-ether anesthesia for seven hours. Mild persistent residual signs were evident.

Case 7.—A man, aged 22, had nitrous oxide-oxygen-ether anesthe-

sia for appendectomy. There was no episode of difficulty. One year later cerebral disturbances were manifested. After another year he was improving.

Case 8.—A man, aged 20, had a toe nail removed under nitrous oxide-oxygen anesthesia. Nervous instability that had existed before the operation was enhanced by the anesthetic.

Pisetsky[117] (1945) reported a case in which the patient, a man, when 33 years of age had ether for ninety-five minutes for a mastoidectomy. There were no complications during or immediately following operation. He was a "heavy drinker." The day after operation left hemiplegia was noticed. The condition became permanent. Six months later, while intoxicated, the patient was anesthetized for one hour for appendectomy. The anesthesia was "difficult." Three hours after operation he was restless and cyanotic. He was aphasic and had swallowing difficulty and continued restlessness. He was restrained. There was gradual improvement. He was discharged on the twenty-first postoperative day.

Barach and Rovenstine[6] (1945) reported a case of a boy, aged 13, who became markedly cyanotic after one half hour of nitrous oxide anesthesia for reduction of a fractured femur. Oxygen restored the color to normal. The child died on the fifth day without regaining consciousness in a completely decerebrate state.

Hamilton[66] (1945) reported a case of ether convulsions. A boy, aged 9 years and 10 months, was given ethyl chloride and ether for an appendectomy. Convulsions started soon after the ether was added. Anesthesia was deepened, oxygen and chloroform, carbogen, coramine, luminal, atropine, calcium gluconate, and saline solution were used in attempts to control the convulsions. The following day he was still unconscious. On the second day, while he was still unconscious, the arms were stiff. The next day he made mumbling responses to questions. Convulsions continued. Magnesium sulfate, enemas, phenobarbital, and insulin with glucose were tried at various times. Three weeks after the operation there was increased spasticity. An extension frame and physical therapy were used to combat contractures that were developing. About six weeks after operation the spastic condition became less severe. There was gross wasting of muscles. The boy spoke a few words and had the mentality of a young child. "It is suggested that the condition could be accounted for by thrombosis of the superior longitudinal sinus, and it appears unlikely that a complete recovery can be expected."

Among others, Feldman[39] (1945) suggested the use of from 40 to 50 per cent oxygen in dental anesthesia to prevent oxygen want.

Schmidt[129] (1945) in discussing respiratory physiology said: "Direct study of the oxygen consumption of the brain in situ has shown that cerebral metabolic activity runs parallel to cerebral functional activity and that convulsions may lead to cerebral anoxia (with all its consequences) because they increase the oxygen demand beyond the available supply."

Wilson[154] (1946) gave a soldier 0.7 Gm. pentothal sodium in preparation for dental extraction (which was not done). Cyanosis and respiratory arrest were treated with oxygen, carbon dioxide, and artificial respiration. Spontaneous breathing began one hour after cessation. The patient was semiconscious. Violent "jactitation" oc-

curred. The next morning he was drowsy and blind. Seven days later "pins and needles" in the right hand and tremors with spasmodic contractions of the flexors of the forearm developed. The contractions extended to the left arm and left leg. Sixty-seven days later his eyes had improved to "slightly short of normal."

Lenahan and Reed[91] (1947) reported a case of apparent decerebrate rigidity. "The patient, a forty-seven year old white male, entered [the hospital] at 4:30 p. m., October 26, 1944, for repair of a right indirect inguinal hernia. There was an alcohol odor on his breath. . . . His history was negative except for an attack of acute anterior poliomyelitis twenty-seven years earlier, which left no residual damage. . . . Anesthesia was induced with 2.5 per cent of sodium pentothal and supplemented with cyclopropane-oxygen. Induction was difficult and 38 cc. of pentothal was necessary before unconsciousness resulted and cyclopropane-oxygen was given. Throughout the forty-five minutes of actual operation, anesthesia was maintained on cyclopropane 150 cc. and oxygen 300 cc. per minute. Supplementary pentothal was not required during operation. An airway was introduced soon after anesthesia had become established. When the patient left the operating room, his pharyngeal reflexes had returned and the airway was removed. . . . On the way to his room the patient stopped breathing and became very cyanotic. The cessation of breathing with cyanosis lasted about two or three minutes. Artificial respiration was begun at the end of one minute and continued while the patient was being removed from the stretcher cart and after he was put in bed. Administration of oxygen by nasal catheter was begun immediately, together with intravenous saline solution and artificial respiration by the Schaefer prone method continued for ten minutes. The airway was open and a good exchange of air was maintained. In addition to manual resuscitation and the administration of oxygen, 2 cc. each of coramine and metrazol were given intravenously five minutes apart. Plasma was used to replace the saline solution. The patient now began a labored type of breathing. . . . Due to rigidity of the patient's neck and inability properly to visualize the larynx, intubation was not successful. . . . Shortly afterward the patient began to have convulsions which were characterized by aimless movements of the arms and legs. . . . The eyeballs were roving as in anesthesia of the second or early third stage. Profuse diaphoresis was observed, the patient's body feeling cold and clammy. A nasopharyngeal tube was introduced. . . . The tonic and clonic movements continued without ceasing and at the end of one hour 100 mg. of curare . . . was given slowly by the intravenous route. This stopped the convulsions and for the next thirteen and one-half hours curare was given intermittently in sufficient amounts to control them. . . . A Magill intratracheal tube was then inserted.

"Continuous oxygen was administered through the intratracheal tube. . . . Because of the large doses of curare that were necessary to control the convulsions, active breathing was sometimes halted and it was necessary to resort to passive respiration for a few minutes until normal respiration was again established. . . . About sixteen hours after he was returned from surgery, the patient began to respond when spoken to and to complain about the intratracheal tube. It was removed

and a nasal catheter inserted. Twenty-four hours postoperatively the patient was able to void voluntarily, expel flatus, and ask for a cigarette. His speech was thick and slow; his stretch reflexes were hyperactive, but the pathological reflexes were absent. For the edema of the brain cells the neurological consultant prescribed 50 cc. of 50 per cent glucose to be given intravenously every eight hours for six doses. . . . The temperature rose steadily to a peak of 104°F. at 2 a. m. on the first postoperative day, then dropped slowly to normal by the third postoperative day. Thereafter recovery was more or less uneventful." The patient returned to a responsible position. After two years he showed no mental impairment.

Ruzicka and Nicholson[126] (1947), in commenting on cardiac arrest under anesthesia, said: "The revival of cardiac and respiratory activity does not mean that the eventual recovery of these patients is assured. . . . In the presence of clinical signs of severe damage to the brain, abnormalities in the brain usually are not discovered at necropsy. Those patients who recover have a constant loss of memory for events twenty-four hours previous to operation."

Woolmer[159] (1948) reported an instance involving accidental injection of procaine. "Cisternal myelography was to be performed on a woman of 39 suffering from a tumor of the cervical cord. As a result of confusing two similar syringes, 3 c.cm. of 2% procaine (60 mg.) was inadvertently injected into the cisterna magna instead of opaque oil, while the patient was sitting upright in a chair. Within a few seconds of the injection the patient complained that her head felt hot. She lost consciousness during the second minute after the injection. Respiration ceased about a minute later, and remained in abeyance for 45 minutes. All reflexes were abolished and there was a profound flaccid paralysis, but no marked cardiovascular depression. There was extreme cyanosis from the onset of respiratory paralysis until effective artificial respiration was established 5-10 minutes later, and the pulse became feeble towards the end of this period, but regained a satisfactory volume when the anoxaemia was corrected.

"Artificial respiration was maintained by rhythmic insufflation of oxygen through an endotracheal tube, and the patient's condition remained fairly good, in spite of the profound flaccidity. Spontaneous respiration began to return 45 minutes after it had ceased, and was fully re-established in a few minutes. The laryngeal reflex became active ten minutes later. The patient did not regain consciousness, however, and during the next three hours she had a series of convulsions. From then, until she died six days later, the clinical picture was typical of grave neuronal damage following cerebral anoxia, with unconsciousness, convulsions, rigidity, mask-like facies and profound dementia. The histological findings were complicated by the presence of a malignant tumor occupying much of the cord and extending into the brain stem. . . . The tumor may have rendered the neurones abnormally sensitive, but it is clear from a study of Courville's cases that the oxygen lack to which they were subjected could have caused similar damage in healthy neurones. In short, the supposition is that this dose of procaine intra-cisternally was enough to cause profound, but reversible, respiratory paralysis. The irreversible changes which

killed the patient were due to anoxaemia."

In the "Queries and Minor Notes" section of the *Journal of the American Medical Association* (1948) a pertinent question is asked and answered[120]:

"To the Editor:—What are the references to literature regarding cerebral cortical changes that may take place with drop in blood pressure following spinal anesthesia with subsequent acute collapse and cardiac and respiratory failure? The patient recovers after a few minutes; begins to breathe and to have normal heart beat and blood pressure. Is there evidence indicating that such persons through deprivation of oxygen to cortical cells will subsequently lead a vegetative existence without normal consciousness? . . .

"Answer. — Reference has been made many times in the literature to damage to the brain which followed use of various kinds of anesthetics and which resulted from a variety of conditions during anesthesia. . . . A variety of results have been observed. In some cases the patient never regains consciousness and dies ten to twenty hours after resumption of breathing and after the return of pulse rate and blood pressure to satisfactory levels. Also, partial recovery, as well as full recovery, may occur."

Etsten and Himwich[37] (1948) determined the degree of oxygenation of the blood during pentothal sodium anesthesia, "determinations which are to serve as a guideline to the limits of safety. . . . A 1 per cent solution of pentothal sodium was administered intravenously to non-premedicated and non-operative subjects. . . . Arterial blood samples were drawn from the femoral artery while the patient was in the resting state and during the various stages and planes of anesthesia. . . . Thirty-eight observations were made on eleven patients. . . . The intravenous administration of sodium pentothal produces anoxia and an increase of carbon dioxide content in the blood during moderate surgical anesthesia and deep surgical planes of anesthesia. The institution of oxygen therapy by insufflation is insufficient to correct the depletion of accumulation of the blood gases during the deep planes of anesthesia. Supplemental respiration technic of oxygen therapy is the most efficient method that can be instituted during pentothal anesthesia to avoid anoxia and hypercapnia."

Strohl and Sarver[141] (1948) reported a case of a girl, aged 7, who was given cyclopropane for appendectomy. Twenty minutes after the incision was made, it was noticed that clonic movements of the face, arms, legs, and abdominal muscle were present. One grain (0.064 Gm.) of phenobarbital was given intramuscularly. Convulsive movements became more pronounced and persisted for fifteen minutes. At this time cyanosis developed and respirations stopped. Spontaneous respirations started after ninety seconds of artificial respiration. The rectal temperature was 106 F. Convulsions recurred intermittently for forty-eight hours. Alternate coma and excitation continued for nine days. Mental evaluation tests, three months after operation, showed an estimated age of five to ten months. "Movements were uncoordinated and characterized by coarseness, spasticity, cog-wheel rigidity and weakness. The child could not stand or walk. She was discharged one hundred and thirty-six days after the onset of illness."

In addition to the cases included in the preceding sequence, there are, among several newspaper ac-

counts of accidents occurring during anesthesia, two which seem to belong in the group under discussion and which have not yet been identified with cases reported in medical journals.

A law suit[163] was brought against a doctor by the husband of a patient, aged 33. She had been "rendered permanently unconscious by an operation" almost two years before. Ever since the operation she "neither sees, nor feels, nor understands." Pentothal sodium was used as the anesthetic. In the suit the husband claimed that "an air bubble entering the blood-stream. . . . caused anoxemic damage to the nervous system and degeneration of the brain tissue."

In another newspaper account[164] microscopic tests were to be made to determine the cause of death of a woman, aged 38, "who had been unconscious for six weeks after being given an intravenous anesthetic preliminary to a facial operation." Sodium nembutal was used intravenously as a preliminary anesthetic, and 60 units of curare was given to relax the muscles of the throat. "However, a spasm of the larynx occurred and the operation was interrupted twice for administration of oxygen."

In other newspaper accounts of deaths during anesthesia, incidents similar to those recounted in medical journals are common. Details are not sufficient to warrant including them in the present review.

In summarizing their cases, Batten and Courville[9] (1940) have stated the conclusion which may well be drawn for the entire series. "The residual, mental and emotional symptoms vary considerably as to their nature, severity and persistence. Disturbances of consciousness, as coma or stupor, are invariably present. This state is followed by delirium, transitory or recurrent hysterical outbursts, emotional instability, hallucinatory or cataleptic states or mental confusion. In patients who survive, progressive dementia has been reported, although improvement even after weeks or months has also been observed. Psychotic states may be (1) transitory and followed by more or less complete recovery, (2) recurrent, often resulting in more serious demented states or deaths, or (3) progressively downward leading to more or less complete dementia. After the period of anesthesia, irritative motor phenomena (convulsive, muscular twitchings or carphologia) often accompany the mental disturbances. In patients who survive for days or weeks or who live with persistent mental or emotional changes, signs indicative of lenticular damage (athetosis, choreiform movements and muscular rigidity) are commonly seen. Alcoholism seems to predispose to cortical damage, resulting in the development of serious, often persistent, nervous or mental states, possibly due to the preliminary interference with cellular respiration. It is likely that cerebral and lenticular damage are due to the accompanying asphyxia (anoxic anoxemia) and not to the toxic effects of nitrous oxide itself. In patients who die within a few days or weeks, patchy necrosis or subtotal destruction of the cerebral cortex is found, often associated with necrosis of the lenticular nuclei. Similar but less extensive changes are found in the brain of individuals who survive for a longer interval."

COMMENT

Having read the summaries of these reports totaling more than 170 cases (in which accurate counts

were given), it becomes apparent that the problem of anoxia during anesthesia is one with which every anesthetist must become familiar. That no such case has occurred in the experience of any one anesthetist is either a case of failure to recognize the condition or extreme good fortune. It is imperative that every person administering anesthetics know every sign of oxygen want and do everything possible to prevent its occurrence. If, in spite of every precaution, anoxic manifestations do appear, immediate corrective measures must be instituted.

False security will be the result of placing confidence in any agent or method on the assumption that anoxia does not exist with its use. In the reported cases, the agents, nitrous oxide, chloroform, ether, ethyl chloride, ether-chloroform mixtures (E_3C_1), ethylene, vinethene, cyclopropane, nembutal, pentothal sodium, avertin, procaine, nupercaine; and the methods, open, semi-open, carbon dioxide absorption, rectal, intravenous, spinal, and combinations thereof have been used.

The common factor seems to be anoxia, the least serious consequence of which it is wise to avoid, and to the more serious consequences of which no person would, for lack of knowledge, risk having contributed.

This review has been prepared with the object of emphasizing a great danger inherent in the practice of anesthesia and of economizing the time and efforts of those who wish to learn more about this phase of the complex science of anesthesia. Additional references will be added in a subsequent report that will also include the reports of anoxia in relation to fetal and postnatal life.

SUMMARY

A review has been made of the literature pertaining to the cerebral effects of anoxia, with emphasis on their occurrence during anesthesia. The deleterious effects of oxygen deprivation were recognized long before the mechanisms were understood. The acceleration of interest during the last fifteen years is a healthy trend. The appalling consequences of anoxia are such that there cannot be overemphasis of the problem in any of its phases.

Note: In attempting to review the cases, it became apparent that true evaluations of the incidence of any complication cannot be made. The report of a single case, without indicating the total experience of the author or the percentage incidence of the episode within his experience, makes it impossible to correlate the facts properly. If a code—e.g., *x*, representing the number of cases reported; *y*, representing the number of the same type of anesthetic; and *z*, representing the total number of cases in the experience of the author, as (1/421/10,000)—could be used in all case reports, eventually the relative importance of any factor could be established.

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163. Charleston, S. C., *Evening Post*, May 28, 1948.
164. Toledo, Ohio, *Blade*, July 5, 1948.

NOTES

When anesthetists get together, they talk about anesthesia. They talk about gadgets, special technics, and interesting cases. This section of NOTES was originated so that anesthetists could exchange ideas in writing as they do in conversation. Send in your contribution now. Other anesthetists will be helped by it.

The Administration of Oxygen with Insufflation Ether.—We, as anesthetists, realize the importance of adequate oxygenation to all living matter. In recent years clinical studies and scientific research in the field of oxygen therapy have constantly been broadening, and, as a result of these studies, the importance of early and adequate oxygenation has taken tremendous strides and is now well established.

For the past year, at General Hospital and at Children's Hospital at Cincinnati, Ohio, we have been giving oxygen to all our patients who are receiving insufflation ether. It is our belief that it has proved most successful. Added to this the surgeons seem more than satisfied with this technic.

The types of cases in which oxygen is given with insufflation ether are tonsillectomies and adenoidectomies, nose and throat operations, dental procedures, all plastic surgery on the head and neck in infants —such as operations for harelip, cleft palate, excision of scars, hemangiomas, etc., — and neurosurgical and eye operations in infants. (Older children are intubated for these procedures.)

Our primary purpose for giving oxygen to all our patients who are on insufflation ether is, of course, to prevent the consequences of obstruction. This obstruction may be due, as we all know only too well, to the mouth gag, the pushing of the tongue back into the pharynx, or to blood or secretions in the pharynx. It is because of these conditions that we treat these children as potential anoxic patients.

Our method of administration is this: The one small end of a Y tube is connected to the vaporizer of the Bellevue Unit, and the other small end to the tubing from the portable oxygen carrier, which is equipped with a regulator. The long end of the Y tube is connected to the tubing with the insufflation hook. Oxygen is turned on to deliver approximately 500 cc. per minute. Another advantage of this procedure is that in case an emergency arises oxygen is ever ready at your finger tips.—Lucille Platt, R.N., Instructor of Anesthesia, Children's Hospital, Cincinnati.

Metubine Iodide.—Metubine Iodide is the latest curare preparation to be placed on the market. It is manufactured by Eli Lilly and Company and is available in 10 cc. vials. Metubine Iodide is a sterile, isotonic, aqueous solution. Each cubic centimeter of the drug is assayed to 20 head drop units, and each cubic centimeter contains 0.5 mg. of the active curare agent, whereas *d*-

tubocurarine chloride contains 3 mg. of the active curare agent per cubic centimeter. The drug has a selective action on skeletal muscle similar to that of *d*-tubocurarine chloride but has the advantage of seldom depressing the respiratory system.

The action of curare at the myoneural junction, blocking efferent impulses, has been recognized for some time, and the drug has been used since 1942 during inhalation anesthesia for relaxation of abdominal muscles. There have been few instances reported that *d*-tubocurarine chloride produces toxic cerebral or cardiovascular manifestations, but the drug frequently produces moderate to severe respiratory depression. This depression was severe enough to instigate research in an effort to find a suitable synthetic compound that would eliminate respiratory depression.

Pharmacologists described the drug as far back as 1938 and stated that it was eight times more potent than *d*-tubocurarine chloride. Clinical work was apparently not engaged in, however, until the spring of 1948, when Eli Lilly and Company placed a quantity of Metubine Iodide at the disposal of the anesthesia department of Indiana University School of Medicine. Dr. V. K. Stoelting,[1] director of the department of anesthesia, reported on a series of 225 cases. He made the early observation that Metubine Iodide did not appear to affect the muscles of respiration unless massive doses were given. Of this series of 225 cases, he reported only fifteen instances of mild respiratory depression, two of which could be attributed to the drug. Dr. Stoelting also reported that the relaxation produced by the initial dose of Metubine Iodide was sufficient for surgical procedures lasting sixty to ninety minutes. After this period, it was sometimes necessary to supplement the dosage with 1-2 cc. of the drug.

The degree of relaxation obtained with the use of Metubine Iodide compares favorably with that obtainable with *d*-tubocurarine chloride. Metubine Iodide is similar to *d*-tubocurarine chloride in that it has no effect on the central nervous system and causes no appreciable change in the blood pressure or heart rate. The contraindications for its use are the same as those for *d*-tubocurarine chloride, namely, respiratory embarrassment, renal impairment, and myasthenia gravis.

The dosage of Metubine Iodide varies with the anesthetic agents used. The manufacturer suggests an average dosage of 4 cc. with cyclopropane, 3 cc. with ether, and 6 cc. with nitrous oxide.

Since obtaining a supply of the drug, I have used it in twenty-five selected cases. This is a brief outline of one of the more interesting cases.

A woman, aged 42, was admitted in profound shock. She gave a history of sudden sharp abdominal pain twenty-two hours previously, and a diagnosis was made of a ruptured ectopic pregnancy. On admission she had an acute upper respiratory tract infection. Systolic blood pressure was 40 mm. Hg; pulse 140; respirations 36; rectal temperature 97 F; red blood count 2,000,000; hemoglobin 30 per cent. The urine contained albumin.

Treatment for shock was instituted immediately. Oxygen was given by nasal catheter at the rate of 6 L. per minute. She was placed in shock position, and 1,000 cc. of whole blood was given rapidly. After an hour, the blood pressure had increased to 90/60 mm. Hg, and her pulse had slowed to 124. Respirations remained at 36.

It was necessary to avoid any respiratory depression, since the hemoglobin

1. Stoelting, V. K.; Graf, J. P., and Vieira, Z.: Dimethyl ether of *d*-tubocurarine iodide as an adjunct to anesthesia. Proc. Soc. Exper. Biol. & Med. **69**:565-566, 1948.

was so low. Atropine, gr. 1/150, was given for premedication. Induction was with cyclopropane, with a high percentage of oxygen, and with use of the circle filter. After lower plane I of anesthesia was established, she was given 5 cc. of Metubine Iodide, just as the skin incision was made. By the time the surgeon was ready to enter the peritoneal cavity, there was satisfactory relaxation. There was no noticeable change in rate or depth of respiration, and a blood pressure of 90/60 mm. Hg was maintained. Another 500 cc. of blood was administered during the procedure. The operation lasted eighty minutes, and it was not necessary to repeat the injection. The patient was responding at the close of the procedure and was awake by the time she reached her room. The postoperative course was uneventful, and seven days later she was discharged.

Summary

Metubine Iodide produces skeletal muscle relaxation comparable to that produced by *d*-tubocurarine chloride, but has little effect on the muscles of respiration. A smaller amount of the active curare agent is actually given when therapeutic doses of Metubine Iodide are used, than when *d*-tubocurarine chloride is used.—Dorothy E. Finley, R.N., Chief Anesthetist, Holzer Hospital, Gallipolis, Ohio.

Reduction of Operating Room Explosion Hazards.—Nylon has been found to have certain advantages over other materials for valve seats for regulators used for oxygen therapy and anesthesia apparatus. Nylon has good elasticity, is not brittle, and has good resistance to abrasion. In the presence of pure oxygen it is much safer than other known and tested materials.

A lubricant compounded from flurine is being used on anesthesia and oxygen therapy equipment. The new compound is claimed to be absolutely nonexplosive.

On May 16 at a meeting of the National Fire Protection Association, the Hospital Operating Room Committee recommendations for revising minimum standards will be taken under consideration. These include: (1) elimination of requirements for explosion-proof ceiling, (2) elimination of requirements for explosion-proof hanging surgical light, (3) elimination of ventilation requirements, and (4) reduction of zone of hazard for electrical installations to a height of five feet. The new requirements will call for conduction flooring throughout the greater part of the surgical suite.

Margaret Sullivan, chief nurse anesthetist at Roosevelt Hospital, New York City, will represent the A. A. N. A. at the May meeting.

LEGISLATION

Emanuel Hayt, LL.B.*

A. Int. No. 3030, Schuyler, includes in definition of practice of medicine the administering of anesthesia, and permits podiatrists, dentists, veterinarians, optometrists and graduate nurses to administer it. (New York)

This bill would amend the Education Law to include the administration of anesthesia as the practice of medicine and defines anesthesiology as the study and practice of the art and science of anesthesia and all its forms and the administration thereof through inhalant, nerve block, fluid therapy or other method.

No person will be permitted to practice anesthesiology unless he or she has been licensed by the State Department of Education. The Board of Medical Examiners will submit to the Department a list of suitable questions for examination of an applicant.

The law would not apply to registered professional nurses who have administered anesthesia under the supervision of a duly licensed physician prior to the effective date of the act; nor to a graduate of a school of nursing which teaches the administering of anesthesia, registered by the Department and who graduated prior to July 1, 1953 and was thereafter licensed to practice as a registered professional nurse.

* * * *

This bill was reported defeated in committee on March 15, 1949. In the interval, objections had been filed by the American Association of Nurse Anesthetists, the New York State Association of Nurse Anesthetists, and the Greater New York Hospital Association.

*Counsel for A.A.N.A.

LEGAL OPINION.—If the surgeon in the operating room disagrees with the medical anesthetist as to the anesthetic to be used, whose judgment should prevail?

Each medical practitioner is a specialist in his own field; the medical anesthetist should not tell the surgeon what operations to perform and the best way to do them, nor should the surgeon advise the medical anesthetist what anesthetic is best suited for the patient.

However, it may be that the medical anesthetist failed to make a preanesthetic examination of the patient and may, therefore, know less about the patient's condition than the surgeon who has examined him.

It should be a rule of the hospital that both the medical anesthetist and the surgeon should make a preanesthetic examination together and agree upon the anesthetic or anesthetics before the patient goes into the operating room. In the case of the nurse anesthetist, the decision of the operating surgeon as to the anesthetic to be used should be conclusive.

NURSES MUST BE CAREFULLY CHOSEN[1].—The patient while under the influence of an anesthetic in a Mississippi hospital was badly burned about the arm by hot water bottles placed by the nurses in charge. Suit was brought against the hospital.

The hospital was a charitable organization. In Mississippi the hospital would be liable only for

1. International Order of Twelve Knights & Daughters of Tabor in Mississippi v. Barnes, etc., Mississippi Supreme Court, Nov. 22, 1948, 17CCH Negligence Reports 406.

negligence in the selection of its nurses; it cannot be held responsible merely on the ground that the employer is liable for the acts of the employee. It is therefore a matter for the jury to decide whether the hospital exercised reasonable care in the selection of the particular nurses whose ministrations resulted in injury to the patient, together with the issue whether or not the injuries were due to the negligence of a nurse of whose incompetence the hospital knew or should reasonably have known.

Not Liable for Burns[2]. — The patient in a New York case had entered the hospital to undergo an abdominal operation. She had returned to her room after the operation under spinal anesthesia and was being given an intravenous injection when she complained to the attending doctor of feeling cold. At the doctor's direction, a hospital nurse procured hot water bottles, and the doctor and nurse placed the bottles in the patient's bed adjacent to her feet. The patient suffered a number of third degree burns from the hot water bottle. It was the patient's contention that the negligence of the hospital arose out of the failure of the attending nurse to heed complaints of the patient and that the failure on the part of the nurse was an administrative act for which the hospital, which was a charitable organization, was liable.

The patient recovered a judgment in the Trial Court for $15,177.45. From that judgment, the hospital appealed. The Appellate Division, after stating that a charitable hospital is not liable for the negligence of a doctor or nurse acting in a medical capacity, though it is liable for the administrative acts of its servants, concluded that the use of hot water bottles was a medical or professional service and that any failure of the nurse to remove the bottles was likewise medical or professional service for which the hospital was not liable. The Appellate Division reversed the judgment of the trial court and dismissed the complaint. The Court of Appeals affirmed the dismissal of the complaint.

Technical Language Not Necessary[3].—The charges against two physicians in Tennessee who were sued for malpractice causing the death of a patient were that they were negligent in failing to take a case history before the operation; to make a preoperative examination; to examine the heart or to take the blood pressure; to take a blood count; to make a blood test for bleeding; to have a urinalysis made; to make necessary and proper examination to determine the type of anesthetic that was suitable to be used; to properly observe the patient while under the influence of the anesthetic which they had administered; to take precautions to prevent loss of blood; to provide postoperative care. These acts, singly or jointly, were alleged to have caused the death while the patient was unconscious under the effects of the anesthetic and the operation.

The doctors sought to have the complaint dismissed because there was no declaration in medical language as to the specific cause of death. Usually the person sued is entitled to know what is claimed to have been the cause of the injury.

2. Sutherland v. New York Polyclinic Medical School and Hospital, Court of Appeals of New York, Oct. 22, 1948, 298 N. Y. 682, 82 N.E. 2d. 583.

3. Moore, Admx. v. Bell etc., Tennessee Supreme Court, Dec. 11, 1948, 16CCH Negligence Reports 419.

Here, however, there was greater knowledge on the part of the doctors. It is not necessary that technical language be used by the plaintiff to describe the cause of the death; it is sufficient that lay language is used. Proof of any one of the allegations as to the cause of death is sufficient. The court held the complaint entitled the party suing to have a trial to prove the alleged negligence of the doctors.

EXEMPTION OF BOARD AND MEALS. — For Federal income tax purposes, the value of meals and lodging furnished to an employee by his employer depends upon all of the facts in each particular case, and no general ruling can be made applicable in all cases.

The gross income of an employee ordinarily include gains, profits, and income derived from salaries, wages, or compensation for personal services of whatever kind and in whatever form paid (Sec. 22(a) of the Internal Revenue Code).

Ordinarily, meals furnished to an employee will be considered compensatory, and the value thereof is includable in the gross income of the recipient. However, if it is shown that the meals furnished to an employee *are for the convenience of the employer, and not compensatory,* the value thereof need not be included in the gross income of the recipient.

As a general rule, the test of "convenience of employer" is satisfied if meals are furnished to an employee who is required to accept such meals in order properly to perform his duties and if the value thereof does not constitute part of the compensation paid for his services.

To exempt the value of meals provided by the employer, it must be shown: (1) that the employer requires the employee to accept the meals provided by him, (2) that because of the nature of the work it is necessary for the employee to accept the meals provided by the employer in order to perform his duties properly, (3) that the employee does not accept the meals furnished by the employer merely because he finds it more convenient to do so by reason of transportation or similar difficulties, (4) that the employer does not furnish the meals merely because he finds it a convenient way of making partial recompense to an employee who could secure meals elsewhere and still give proper attention to his duties.

The Research Institute's Federal Tax Coordinator, published January 28, 1949, adds that "board and lodging for employees is the target of a new Bureau crackdown. Until recently, many employees have been excluding from their taxable income the value of meals and quarters furnished by their employers. Reason for the exclusion has been the Bureau's 'convenience of employer' rule: if the employee is required to accept the facilities to perform his duties properly, their value is not income.

"The rule hasn't changed, but the Bureau's attitude in applying it definitely has. Chief test will now be whether the arrangement to furnish board and lodging is compensatory in nature. If so, the convenience of employer rule won't apply. Since most of these arrangements have both a compensatory and convenience of employer element, the Bureau's new approach will be a blow to the vast majority of employees who've been treating their board and lodging as nontaxable."

THE NEWS

PROMINENT CONGRESSWOMAN TO BE BANQUET SPEAKER

Clinics Planned in Cleveland Hospitals

Frances Payne Bolton, Congresswoman from Cleveland, has accepted an invitation to speak at the A. A. N. A.'s annual banquet. Mrs. Bolton has been the sponsor of numerous bills to aid nursing. She was the author of the Bolton Nurse Training Act that subsidized basic and advanced nurse education during World War II.

The A. A. N. A.'s Award of Appreciation will also be presented on this occasion. The award is given annually to a person or institution that has made an outstanding contribution to the advancement of nurse anesthetists.

The sixteenth annual meeting of the A. A. N. A. will open officially with the opening of the fifty-first convention of the American Hospital Association on Monday, September 26. General sessions will be held at the Public Auditorium, Cleveland's convention hall. The Public Auditorium is within walking distance of the Association's headquarters at the Hollenden Hotel.

A one and a half day meeting of the Assembly of the Directors of Schools of Anesthesia is scheduled to begin on Sunday, September 25, at the Hollenden. Although the program of the assembly is primarily of interest to school directors, all Association members are invited to attend.

The annual business session is scheduled for Tuesday, September 27. At this session, revisions of the Association's bylaws will be presented for discussion and vote. Reports of the work of the Association during the year will be presented by officers and committee chairmen, and trustees and officers for 1949-50 will be elected.

Membership Tea

A tea for all Association members is being planned for Tuesday afternoon to give the members an opportunity to meet the new officers and trustees. The Ohio Association of Nurse Anesthetists is making arrangements for the tea, and Ohio members will serve as hostesses.

General Sessions

Four general sessions are scheduled to be held during the convention, one each Monday and Wednesday and two on Thursday. Clinics have been arranged for Wednesday morning at the University Hospitals, Cleveland Clinic Hospital, and Cleveland City Hospital. An outstanding feature of the program will be a forum on anesthesia for patients with complex medical problems. Donald Hale, M. D., anesthesiologist at the Cleveland Clinic, will be the moderator, and members of the clinic

staff will participate. The complete program will be published in the August JOURNAL.

The committee in charge of local arrangements is composed of Gertrude Fife, chairman, Ann Dickerson, Helen M. Heckathorn, and Marjorie Pearce.

A large attendance is expected for this sixteenth annual meeting, and members are urged to make reservations promptly. On page 186 of this JOURNAL is a form to be used in applying for reservations.

The Convention City

As a convention city, Cleveland offers many attractions and points of interest. All major hotels, the shopping district, transportation points, amusements, Lake Erie, and the Public Auditorium are within a few minutes' walking distance. Any point in the city is easily accessible from the downtown area.

At the hub of the city's business activities is the Public Square, a small clearing of land which was purchased by the Connecticut Land Company in 1795 for $1.76 and which is now a modern business and transportation center valued at more than $20,000,000.00. Towering over the square is Cleveland's familiar landmark, the 52-story Terminal Tower, with an observation room on the forty-second floor that affords a splendid view of the city. It is the seventh tallest building in the world, the other six being in New York. Other parts of the Terminal unit are a railroad station, a large department store, a modern hotel, and several shops.

The Mall, which overlooks Lake Erie and extends into the heart of the business district, is made up of seven great buildings. The $10,000,000 Public Auditorium, the Federal Building, the Public Library, the Board of Education Building, City Hall, Cuyahoga County Court House, and the lakefront Municipal Stadium seating 83,000 are included in the Mall Development.

The Public Auditorium has three theaters, ten halls seating 75 to 500 each, and many committee rooms and offices. The main auditorium seats 12,500; the Music Hall seats 3,000 and can be thrown together with the main hall so that 16,000 can watch the action on the 5,000 square foot stage.

Cleveland ranks among the nation's outstanding cultural and educational centers. Western Reserve University, comprising various colleges, is one of Ohio's oldest collegiate institutions. Case Institute of Technology, adjoining the campus of Western Reserve, is among the country's top engineering schools. The two institutions occupy high ground overlooking Wade Park. Other Cleveland collegiate institutions are John Carroll University and Fenn, Ursuline and Notre Dame colleges.

Among the city's cultural institutions are the Cleveland Museum of Art and Severance Hall, both located in University Circle overlooking Wade Park. Other famous institutions in Cleveland include the Museum of Natural History, the Western Reserve Historical Society Museum, Dunham Tavern, the Public Library, the Health Museum, Brookside Zoo, and Nela Park University of Light.

OHIO OFFICERS

Elizabeth Boyer, Crile General Hospital, Cleveland, was re-elected president of the Ohio Association of Nurse Anesthetists at the association's annual meeting in Colum-

bus, March 23-24. Also re-elected were Sr. John Edward, 1st vice president, and Rosemary Curran, 2nd vice president. Lucy E. Richards is the new secretary-treasurer. Lucille M. Platt was elected trustee.

A revision of the state association's bylaws provides for a committee on publications and publicity. This committee will undertake the publication of a state news bulletin.

A gift of $300 was voted by the members to the Agatha Hodgins Educational Fund, in addition to the state's share of the former Trust Fund.

WESTERN STATES SECTION MEETING IN SAN FRANCISCO

A feature of the nurse anesthetists' section of the Western Hospitals Association convention in San Francisco, May 9-12, will be a forum on "Harmony in Anesthesia." Moderator of the discussion is to be Jane Osborne, Peralta Hospital, Oakland. To be represented on the panel are the American College of Surgeons by Dr. W. W. Washburn; hospital superintendents by Mr. Orval Booth; medical anesthetists by Dr. Fenimore Davis; nurse anesthetists by Josephine Bunch. At a luncheon meeting on Monday, Grace Gurnea, chairman of the public relations committee of the California State Nurses Association, will speak on "The Anesthetist and Human Relations." Edna Peterson is chairman of the nurse anesthetists' section.

CALIFORNIA ELECTS OFFICERS

The annual business meeting of the California State Association of Nurse Anesthetists was held at St. Mary's Hospital, San Francisco, on March 25. Officers elected were: Jane Osborne, president; Marie Callori, 1st vice-president; Mary Thornton, 2nd vice-president; Ursula Heitmeyer, secretary; Florence Lueck, treasurer; Edna Peterson and Cleo D. Bopp, trustees.

MIDDLE ATLANTIC ASSEMBLY HOLDS FIRST MEETING

The newly formed Middle Atlantic Assembly of Nurse Anesthetists will convene for its first annual meeting on May 18, 1949, in Atlantic City, with headquarters at the Ritz-Carlton Hotel. The three day session of the New York, New Jersey, and Pennsylvania associations is to be held in conjunction with the convention of the Middle Atlantic Hospital Association. Alice Lamberson is president pro tem. of the assembly, and Emma A. Miller the program chairman.

Preconvention meetings of the board of directors of the participating associations are scheduled for Wednesday morning, the convention to be formally opened Wednesday afternoon. At the opening session, Miss Lamberson and Myra Van Arsdale, president of the A. A. N. A., will give greetings. Ellis K. Hultzman, M. D., director of anesthesiology, Jewish Hospital, Philadelphia, will discuss "Newer Aspects of Anesthesia in Geriatrics," and Anthony F. Gorman, D.D.S., chief of oral surgery, Cooper Hospital, Camden, N. J., will speak on "Anesthesia in Oral Surgery."

Business meetings of the participating state associations are planned for Thursday morning. On Thursday afternoon, the delegates will reassemble for a business meeting of the assembly.

CALENDAR OF COMING EVENTS

May 9-12	Western States Assembly of Nurse Anesthetists, San Francisco
May 18-20	Mid-Atlantic Assembly of Nurse Anesthetists, Atlantic City
May 19	Annual Meeting, Pennsylvania State Association of Nurse Anesthetists, Atlantic City
May 19	Annual Meeting, New Jersey State Association of Nurse Anesthetists, Atlantic City
May 19	Annual Meeting, New York Association of Nurse Anesthetists, Atlantic City
May 21	Annual Meeting, Georgia Association of Nurse Anesthetists, Atlanta
May 26-27	Upper Midwest Assembly of Nurse Anesthetists, Minneapolis
September 26-29	SIXTEENTH ANNUAL MEETING, AMERICAN ASSOCIATION OF NURSE ANESTHETISTS, Cleveland

On Friday, the subjects to be discussed include: "Pentothal Sodium for Head and Neck Surgery," Olga Schweizer, M.D., director of anesthesiology, Memorial Hospital, New York City; "The Use of Pentothal Sodium with Curare in Plastic and Ophthalmic Surgery," Louise Tyler, R.N., chief anesthetist, St. Michael's Hospital, Newark; "Anesthesia in Intestinal Obstruction," Mario Troncelitte, Jr., M.D., chief of anesthesiology, Pennsylvania Hospital, Philadelphia; "Basal Narcosis in Children," Joseph F. Artusio, Jr., M.D., associate professor of surgery (anesthesiology), Cornell University Medical College.

DEATHS

Mary K. Dimig of Portland, Oregon, a member of the Oregon Association of Nurse Anesthetists, died on February 12, 1949, after a long illness. Miss Dimig received her training as a nurse at Atlanta Hospital, Atlanta, Iowa, and postgraduate training at Grace Hospital School of Anesthesia in Detroit. Miss Dimig was head of the anesthesia department at the Emmanuel Hospital of Portland for twenty years, until her illness two years ago.

Jean E. Dow of Portland, Oregon, died on February 24, 1949. Miss Dow had been a member of the Oregon Association of Nurse Anesthetists since 1936, having taken her postgraduate training in anesthesia at St. Vincent's Hospital in Portland.

Alice Madge Riley, a member of the Florida Association of Nurse Anesthetists, died on February 21, 1949, in Philadelphia after an illness of several months. She was graduated from the Northeastern Hospital School of Nursing in Philadelphia and took training in anesthesia at the Broad Street Hospital in Philadelphia in 1924. For the past six years she was chief anesthetist at St. Luke's Hospital, Jacksonville, Fla.

Sister Ella H. Risser, a past president of the Kansas State Association of Nurse Anesthetists, died on March 27, 1949. At an early age she joined the order of the Mennonite Sisters. After her graduation from the St. Joseph's Hospital School of Anesthesia in Chicago in 1938, she was anesthetist at the Bethel Deaconess Hospital in Newton, Kansas.

ABSTRACTS

HERSHENSON, B. B.: Premedication and anesthesia in obstetrics. Current practices at the Boston Lying-in Hospital. New England J. Med. **239**:429-433, Sept. 16, 1948.

"At the Boston Lying-in Hospital, there has been an evolution through various developmental phases of the subject. The keynote has always been the practice of safe relief of pain, permitting the obstetrician to carry on a conservative policy in the conduct of labor. All the known regional and inhalational anesthetic agents and technics have been employed, and all routes of the body have been utilized for the introduction of amnesic and analgesic drugs. . . . The greatest emphasis should be placed on the knowledge, experience, skill, judgment, attention and mutual professional confidence of the members of the obstetric team rather than on the agent or technic employed. Secondly, the complete individualization of selection of agents, dosage and routes of administration in the able hands of a well trained team of obstetrician and anesthesiologist is the only true path to safety. Thirdly, the ideal agent or combination of agents is not available to meet all the requirements necessary for safe, controllable and effective obstetric amnesia, analgesia and anesthesia. Finally, we have been impressed with the fact that our most successful methods have included the use of scopolamine. . . . Over 80 per cent of our deliveries are completed under inhalation anesthesia."

BEATON, DONALD: Pethidine in labour. Edinburgh M.J. **55**:354-361, June 1948.

"In assessing the value of a new drug, whether clinically or experimentally, it would seem preferable to use that drug alone and not to obscure its effect by the concurrent use of another. This is particularly so in the use of pethidine, the effect of which on the duration of labour is still under review and its pharmacological action in labour still undecided. . . . Ninety pethidine cases and 90 controls are now available for study, having been delivered at the Cressweil Counties Maternity Hospital within the past six months.

"I set out in this survey to see if there would be value in extending this series and if the methods could be improved. I propose to continue because certain features have been found which are contrary to the findings of other observers. The method will be altered the better to assess the duration of labour, necessitating vaginal estimation of the degree of dilatation of the cervix in both groups, pethidine and control. Since there was no puerperal morbidity in either group in the pilot survey, it is suggested that routine vaginal examination is not detrimental to the patient, although contrary to the practice of this hospital. Hereafter the administration of pethidine will be postponed till the patient is beginning to complain of pain and not before the cervix is 2-3 fingers dilated, otherwise the plan remains unchanged. Most of the impressions gained, some of which have been tentatively confirmed by critical analysis, have been in accord with the findings of previous writers except that pethidine does not appear to shorten labour. It has no serious ill-effects on mother or child except that the incidence of post-partum hemorrhage appears to be increased. In this series the drug has been used with great advantage to the mothers, particularly those who were nervous and excited. There appears to be

safety in large dosage no matter at what time in the first stage of labour the drug is given."

GREGORY, RAYMOND, AND LEVIN, W. C.: Studies on hypertension. VII. Mechanism of the fall in arterial pressure produced by high spinal anesthesia in patients with essential hypertension. Arch. Int. Med. **81**:352-363, Mar. 1948.

"Simultaneous arterial and venous pressures were determined in 5 normotensive subjects. Twelve separate studies were made in 10 patients with a clinical diagnosis of essential hypertension. Control observations were made, and similar determinations were then made with high spinal anesthesia induced by 150 mg. of procaine hydrochloride. Observations were continued during recovery stages. . . . In the majority of patients with essential hypertension, the arterial pressure fell before the venous pressure fell. In 1 case, the venous pressure fell without any significant decrease in arterial pressure. In only 2 cases, the venous pressure dropped first, and in these 2 cases the arterial pressures fell to their lowest levels before the venous pressures fell to their lowest levels. In these 2 cases, the arterial pressures were rising while the venous pressures continued to fall. There is no constant time correlation between the falls of arterial and venous pressures during high spinal anesthesia in patients with hypertensive disease. The changes in arterial and venous pressures described are probably not causally related. It is extremely unlikely that decreased venous return and diminished cardiac output are the causes of the fall in arterial pressure caused by high spinal anesthesia in either normotensive or hypertensive subjects."

MAKE YOUR HOTEL RESERVATIONS NOW!
for the
SIXTEENTH ANNUAL CONVENTION
September 26-29, 1949
Cleveland

Applications for hotel reservations may be obtained by filling out this form and returning it to:
The Executive Office
American Association of Nurse Anesthetists
22 East Division St.
Chicago 10, Ill.

Name.....

Address.....
(street) (city) (state)

If you wish to be assigned a room with another person, please give her name below:

Name.....

Address.....

She is....., is not....., a member of the Association.

She has....., has not....., expressed her willingness to share the room.

EACH PERSON MUST FILE A SEPARATE APPLICATION.
APPLICATIONS SHOULD BE MADE BEFORE JULY 1.

BOOK REVIEWS

NURSING FOR THE FUTURE. By Esther Lucile Brown, Ph.D., Director, Department of Studies in the Professions, Russell Sage Foundation. Cloth. 198 pages. New York: Russell Sage Foundation, 1948. $2.00.

For a half century, there has been a periodic resurgence of interest in the grading of nurses and the accrediting of schools of nursing as a cure-all for the problem of fitting into modern society a service with tradition rooted in the Middle Ages. The most recent panaceas are contained in the Rich Report on the Structure of Organized Nursing and Esther Lucile Brown's *Nursing for the Future.* The latter report was prepared for the National Nursing Council and published by the Russell Sage Foundation. The effect of each on nurses, hospital administrators, and physicians has, to say the least, been explosive. This despite the fact that six nursing organizations sponsored the Rich Report, and that eleven nursing organizations plus the A.H.A. and A.M.A. comprise the constituent bodies of the National Nursing Council. There is also evidence that *Hospital Care in the United States,* a survey financed by the Commonwealth Fund and prepared with the cooperation of the A.H.A., and the Rich Report had a decided influence on the survey made by Dr. Brown.

The stated purpose of *Nursing for the Future,* first, recognizes that "there was something not only drastically but chronically wrong with a system of education which could not meet the demand either for qualitative or quantitative service," and, second, proposes that there should be "an examination of the question of who should organize, administer and finance *professional* schools of nursing." The decision was "to view nursing service and nursing education in terms of what is best for society—not what is best for the profession of nursing as a possibly 'vested interest.'" As "clear a picture as possible would have to be drawn of the probable nature of health services in the second half of the twentieth century, and of the nursing services likely to be demanded by those evolving health services. Next, inquiry into the kinds of training and of academic and professional education requisite to prepare nurses to render those various kinds of nursing services would be essential." "In general, effort was made to visit 'better' schools in every region. Miserable schools of nursing had been seen at sundry times in various places. No virtue was inherent in further examination of what should not be done."

The only fair way to evaluate such a reported survey is to compare the aim with the results. Dr. Brown frankly states that she was handicapped in observing by not being a nurse. A certain amount of leniency is in order when she draws freely from *Hospital Care in the United States* for her picture of the hospital of the future as a public health center for the prevention as well as the treatment of disease. It is regrettable, however, that she chooses fields of exaggerated current popularity as examples of expanding services: psychosomatic medicine, the Grantly Dick Read school of obstetrics, and the problems of emotional development in children. She makes brief shrift of the battle of medical science against

communicable disease, the diseases of middle age—"such as cardiac diseases and cancer"—, and the degenerative processes of old age.

To provide nursing service for the projected future expansion of health facilities, the author first advocates a category of licensed practical nurses. These nurse attendants are "to care for subacute, convalescent and chronic patients and to assist the registered professional nurse in the care of others . . . under the direction of a licensed physician and the supervision of the registered professional nurse . . . in homes, hospitals, institutions, public health agencies, doctors' offices and in commercial and industrial firms.'" It is also advocated that the training of the practical nurse "should be reposed within the public education system, and more specifically within vocational or adult education."

The term *professional* nurse would *"be restricted to those who have been graduated from schools designated as professional* [degree-conferring institutions] *or whose right to be thus considered has been demonstrated through some system of examination; achievement that has been objectively evaluated, such as marked excellence in clinical practice, supervision, administration, teaching, or scientific research and writing; admission to fellowship in an academy of nurses; or by means of other plans devised to raise the status of nursing."*

The fate of the graduate bedside nurse becomes a matter for future decision. Until such time as she is eliminated or fits into "nursing for the future," Dr. Brown recommends the inspection for purposes of accreditation of all schools of nursing, the public to assume a substantial part of the financial burden. In addition, an effort should be made for the creation of central schools of nursing and for the utilization of teaching facilities of junior colleges.

There is no bibliography in the published report, footnote references being limited to the more recent publications. We therefore have no way of knowing whether the author was aware that in 1912-13, for example, the American Hospital Association took under consideration both a licensing of practical and graduate nurses, and a grading of nurses that made room for the college graduate at the top and the household (practical) nurse at the bottom. What happened then would seem to be important information for one who would predict a future situation.

What is to characterize the *professional* nurse of the future and what will be her job?

"These are nurses who will be expected to be fully contributing team members in complex clinical situations, where both technical skill of a high order and psychological and sociological orientation are requisite; in the wide field of community nursing and community health services where prevention of disease and therapy, but more particularly the maintenance of health, are ever-widening goals; in the supervision of the activities of many kinds of assistant and graduate personnel; in planning and administering nursing programs, often within agencies and institutions of great size and complicated organizational structure. Included also are those nurses who must assume responsibility for formulating educational programs; instructing students of nursing, graduate nurses, practical nurses, and other assistant personnel in the content and methodology

of nursing, and in what the student and graduate nurse should teach patients individually and in groups and how this can best be done; carrying on desperately needed research, writing, publication, and consultation related to the improvement and extension of nursing care; planning for the continued growth and development of the nursing profession; and administering those plans in close cooperation with other health services and with the needs of society always in mind."

With regard to the need for technical skill of high order, another statement of Dr. Brown's is pertinent: "A few nurse administrators and educators have become so alarmed at the present and probable future proportions assumed by technical procedures that they assert that immediate relief must be found through making internes or especially trained technicians responsible for a major part of this burden. Unless this be done, they see subsequent deterioration rather than improvement in those aspects of nursing care that depend upon the use of words and of psychological skills."

Dr. Brown outlines the educational needs of this new professional nurse thus: "Two distinct but closely interrelated kinds of preparation that only higher education is broadly equipped to provide are essential for the making of such a nurse. The first is the laying of a foundation that permits continuing growth of many kinds, such as in: positive health and integration of the personality; insight into one's own motivation, the behavior of others, and cultural patterns that condition human behavior; ability to use spoken and written language effectively as a method of communication; skill in analysis of problems, methods of obtaining needed data, and formulation of logical conclusions, principles, or theories; perspective, gained from the historical and anthropological record of human development, of contemporary social institutions and their functions; understanding of and conviction about the rights and responsibilities of intelligent citizenship and membership in a profession.

"The second kind of preparation is the more specifically technical training for professional practice. But this training must transcend that for the care of the hospitalized sick. It must be preparation for the broad field of community nursing service. Besides the other relatively well-defined components of the course of study, should be included understanding of the effect of nutrition, housing, employment, economic income, class and caste structure, recreational activities, and so forth, upon individual and national health; some knowledge of the principles and functions of social work and of how nurses and social workers can most effectively act as a team; experiments in analyzing the health needs of individuals, families, and communities, and in initiating action to meet these needs; and preparation in the art of teaching health to persons, whether sick or well and whether individually or in groups."

One wonders how in the name of common sense such a program could bear fruit—even though the academic and professional training were integrated in an institution of higher learning—in a four or five year course leading to a B.S. degree. Theoretically, the plan is a worthy one. But in view of the parlous state of education, as seen by top-ranking educators, such a comprehensive curriculum could hardly be gelled, even at the graduate level, without revolutionary measures.

The dean of the school of nursing, Dr. Brown proposes, should hold a chair on the level of the dean of the medicine and law faculties, regardless of her academic preparation. "The school must be prepared to meet competitive situations within the university generally, but more particularly in its relations with the medical school and the hospitals from which clinical facilities are obtained."

No data of any kind are given as to the number of each kind of educational undertaking needed or the approximate number of students who should be trained in each. "The very existence of stated estimates for ultimate goals might serve to freeze a situation that is now dynamic and should remain so, at least until more experimentation and experience are available regarding allocation of functions to persons with different kinds of preparation."

What are Dr. Brown's concrete recommendations? "Schools for practical nurses should be developed during the next few years as rapidly as planning for sound establishment and wise distribution will permit; that several hundred socially undesirable hospital schools should be closed; that advanced curricula within universities and colleges should be restudied and greatly strengthened. The desirability of these changes is unmistakable. Equally unmistakable is the need for development and cultivation of basic schools of nursing in institutions of higher learning to go on apace."

There is no question that Dr. Brown's report maps out a kind of nursing for the future and that she examines the question, "who should organize, administer, and finance *professional* schools of nursing." She fulfills her assignment even though, in so doing, she has to distort the true meaning of professional education and impoverishes the time-honored position of the nurse as one who cares for the sick. It would be well for nursing leaders to examine what right the social worker-administrator-research-educator-writer nurse, that Dr. Brown's system purports to produce, would have to call herself a nurse. The crying need — albeit there is a need for university-educated teachers in nursing education —is for intelligent bedside care. Perhaps the common concept of "caring for the sick" is narrow and could legitimately be broadened to include the contribution of the nurse attendant and the *professional* nurse. But it is going to be extremely difficult to shake the belief that any nurse worthy of the name is concerned first with high-grade individual patient care and only secondarily with administrative and educational controls and the supervision of second class helpers.

Nurses should ask themselves whether, in the light of current developments, their leaders are directing them down the road of self destruction. In abandoning the field of routine bedside nursing to the practical nurse, organized nursing should think twice about the potention of organized practical nurses in nursing affairs. If future health programs call for the type of worker Dr. Brown describes as a *professional* nurse, perhaps a whole new category of medical assistants should be created—leaving nursing and the control of nursing to those who want to nurse.

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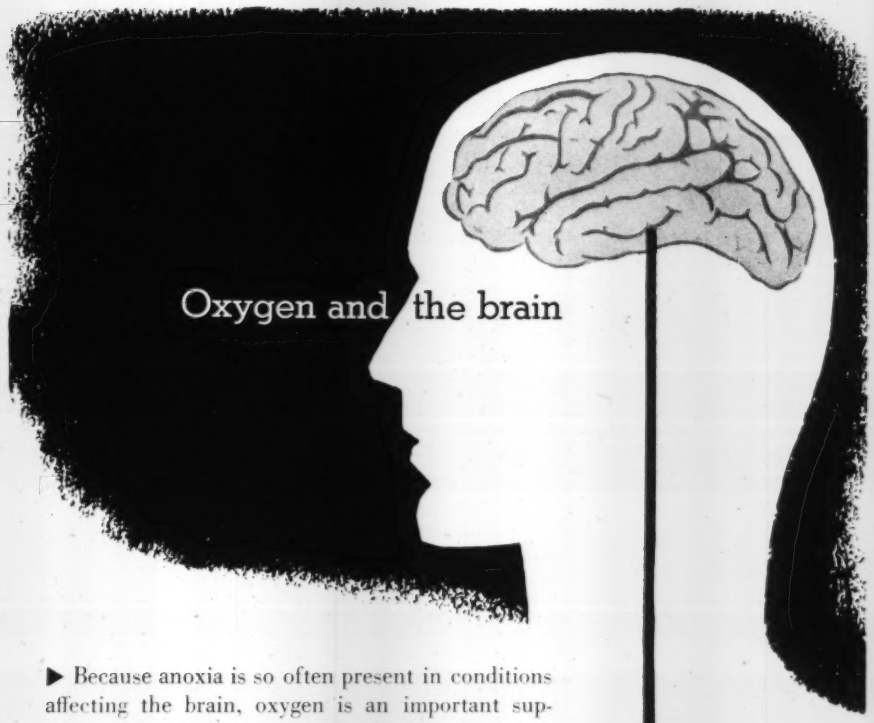

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